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IMMEDIATE CIRCUMCISION OF THE NEWBORN MALE

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C IRCUMCISION is the oldest surgical operation known to man,[1] dating some 6,000 years back into antiquity to the time of Abraham. During these centuries there developed a rough division of peoples in regard to this procedure, between those who followed the custom of the Hebrew and circumcised on the eighth day, and those who circumcised in the thirteenth year after the practice of the Egyptians. It is the purpose of this paper to endorse a possibly more suitable time to perform this operation, namely, immediately after the birth of the newborn.

Our experience with this program dates back to 1941 when, due to the exigencies of World War II, the crowding and bed shortage, and particularly the reduced number of physicians, the first few immediate circumcisions were performed without mishap. Since that time approximately 14,000 newborn males have been circumcised at birth in this hospital, not to include an estimated 10,000 circumcisions performed in the other two Akron hospitals, with no known serious complication. This constitutes a vast number of procedures and the results have been most gratifying.

Method

We have analyzed the records for a representative year, 1950, at Akron City Hospital. During that year there were 3,953 infants delivered, 3,722 of whom were at full term; of the latter, 1,669 were full-term males and of these 1,480 were circumcised at birth and the remaining 269 were either uncircum-

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cised, Hebrew, or electively circumcised at some later time. We have excluded from these totals the prematures, unreportable births, and neonatal deaths and stillbirths as listed in Table II.

TABLE I. CIRCUMCISIONS, AKRON CITY HOSPITAL, 1950

	NUMBER	PER CENT
Full-term male births	1,669	100.0
Uncircumcised males	140	8.4
Total males circumcised	1,529	91.6
Immediate circumcisions	1,480	88.6
Circumcised first day	12	0.7
Circumcised second day	13	0.7
Circumcised thereafter	24	1.4

TABLE II. HOSPITAL STATISTICS, AKRON CITY HOSPITAL, 1950

	NUMBER	PER CENT
Number of infants delivered	3,953	100.0
Number of live births	3,877	98.1
Number of stillbirths	68	1.7
Deaths under two weeks of age	48	1.2
Babies weighing 2,500 grams or less	155	3.9
Number of these who died	25	16.1
Reportable male births	1,993	50.4
Full-term male births	1,669	42.4

The data that were extracted from these records included daily weights, rectal temperatures, mode of delivery, and obstetrical complications that might have affected the infant's well-being during his neonatal life.

The laboratory studies were simple and brief. We recorded approximately 700 bleeding and coagulation time determinations on infants at varying periods of their neonatal life. We define "bleeding time" as that period of time that elapses between puncture of the infant's heel and the absolute cessation of the surface blood flow. "Coagulation time" was determined to the nearest half-minute using the capillary tube method with a minimum strand of 5 mm. We have no argument with the purists in this field who prefer more elaborate methods of study of the blood-clotting mechanism, but Bodansky[2] states that "the rate of blood clotting in the newborn infant roughly parallels the prothrombin time, delayed clotting occurs particularly where there is prothrombin deficiency." Thus, we feel it has a significant value in the comparisons we make.

Indication for Circumcision

Although we do not hold the disdain for the prepuce that Dr. P. C. Remondino does in his enlightening book[1] when he refers to the "tight-constricted, glans-deforming, onanism-producing, cancer-generating prepuce," we do feel that there are many excellent reasons for routinely circumcising the male.

Commonly quoted reasons for circumcision with which we are in full accord are:

    1. Hygienic: Certainly cleanliness is undebatably beneficial.

    2. Phimosis: Actual phimosis and paraphimosis require surgical correction.

    3. Venereal: Approximately 75 per cent of all penile chancres occur on the foreskin and the incidence of penile chancres and gonorrhea is four times greater in the uncircumcised.[3]

4. Cancer: There are no valid reported cases of carcinoma of the penis in a circumcised male.[4]

Those reasons which are rightfully subject to debate include: (a) Circumcision will reduce the incidence of onanism. The venerable authors who discuss this topic are in total disagreement.[1, 5] (b) Circumcision will increase the male libido. The vast progeny of the Jewish males attest to the fact that functionally, at least, performance is not diminished by this operation. This fact, in the days of the Roman Empire, brought havoc to their number and one of the edicts issued from Rome forbade circumcision on the grounds that in this way the Hebrew population would thus be controlled.[1] On the other hand, critics of circumcision[6, 7] flatly state that libido is decreased by the procedure. (c) Longevity, immunity to nearly all physical and mental illness, increased physical vigor, etc., are all attributed to this practice by various authors of the mid-nineteenth century as a result of their studies of the Jewish people (Bernouilli, B. W., Richardson, M. Neufville, et al.). In the minds of these men the entire productivity and vitality of this religious group is attributed to the fact that they were circumcised.

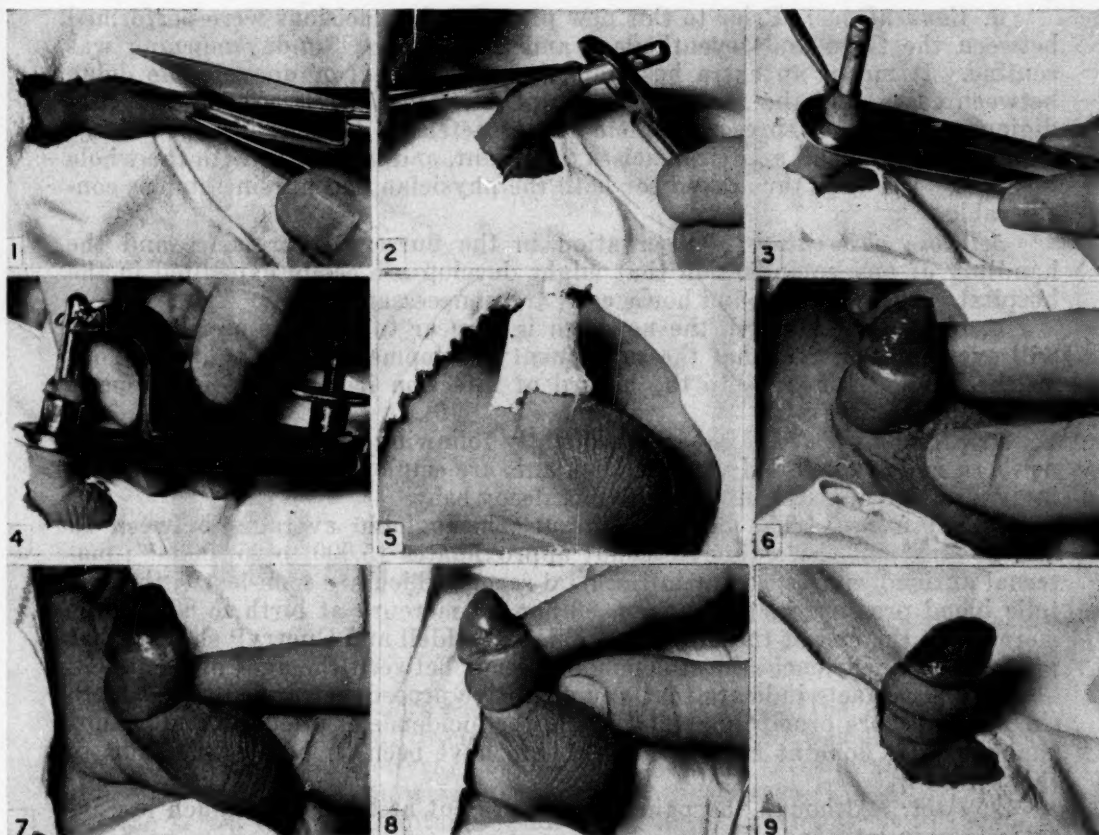Fig. 1.—Gloveless technique.
1. Dorsal slit recommended. *2* and *3.* Simple method of applying clamp. *4.* Prepuce excised without delay. *5.* Petrolatum dressing. *6.* First day. *7.* Second day. *8.* Third day. *9.* Fourth day.

Why Immediate Circumcision?

In addition to the aforementioned reasons for doing the operation, we shall list several reasons to support immediate circumcision.

1. Safety: The safety factor was endorsed by each physician questioned, provided the operation be performed only on full-term, normal, healthy male infants in whom no medical complication is anticipated. This would exclude babies of an Rh-negative multiparous mother.

2. Absence of complications: There were no cases of significant penile infections in this series. There were five cases of postoperative bleeding in 1,480 circumcisions, an incidence of 0.3 per cent. Three of these were controlled by sutures and two by the application of Gelfoam. In each case the technique was at fault, since an obvious defect, usually near the frenulum, was found; each of these babies gained weight normally, fed well, and the circumcision site healed readily. Because of the close observation possible, these babies were treated within two hours of the time of the original circumcision. We use the clamp first described by Yellen[8] and devised by Goldstein,* and most of our operators are reasonably adept (Fig. 1).

3. Healing: These circumcisions are healed in 36 to 48 hours, so that by the time the mother takes her child home there is no dressing on the penis, healing is well advanced, and the danger of hemorrhage and infection negligible.

4. Convenience: Prior to this new plan the circumcisions were performed between the third and seventh days and a line-up on Sunday morning was routine. It meant an extra hospital trip, a good deal of unavoidable delay between cases, and the resulting traffic problem in the birth rooms was prodigious. Under the present regime the obstetrician finishes his episiotomy, walks across the hall and circumcises the infant, and is finished with the whole business. The time thus saved for both the physician and nursing staff is considerable.

5. Close observation: Observation in the nursery, redressing, and the handling of any complication that might develop are easily expedited in the hospital. All home care and house calls are unnecessary.

6. Sterility: At birth the newborn is as near to absolute sterility as he will ever be. We feel that the subsequent development of the bacterial flora on the baby's skin adds to the hazard of infection if the operation is postponed until a later date.

7. Stimulation of the baby: Frequently following a general anesthetic the newborn is depressed and various stimulants are employed; circumcision unfailingly produces an excellent response in a sleepy baby.

8. Physiology: The newborn infant's hemoglobin averages between 19 and 23 Gm. and the leukocyte count approximates 15,000 to 25,000[10, 12]; maternal antibodies are present in the fetal serum which are soon lost[10]; the systolic blood pressure increases from 60 mm. of mercury at birth to 80 mm. of mercury at the end of the first week[9]; also, Waddell and Guerry[11] showed that prothrombin deficiencies most commonly occur between the ages of 48 and 72 hours. These facts indicate that any operative procedure carried out at birth should heal more promptly and with a lower incidence of infection and hemorrhage than if done at a later date. There have been no penile infections in this series.

9. Pain: Although the pain sense is present at birth, it is much less intense than in later infancy.[10]

Effect on Weight Gain

We have studied the weights of these 1,480 babies who were immediately circumcised in an effort to determine whether this procedure adversely affected the normal expected weight gains that have already been established.

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*Manufactured by the Gomco Surgical Mfg. Corp., Buffalo, N. Y.

Stone writes that "the most reliable index of the general well-being of the newborn is the weight curve, and the actual weight gain per day is immaterial . . . it is the 'weight tendency' that is important."[10] Most of the pediatric texts give a normal expected weight loss as averaging about 5 to 8 per cent of the birth weight. One textbook[9] makes this statement: "During the first three days of postnatal life approximately 95 per cent of newborn infants lose 0.2 pound or more in weight. In not more than 25 per cent does this loss exceed 0.7 pound and in less than 2.0 per cent is it more than 1.1 pounds. About 25 per cent of the newborns regain this loss by the end of the first week and about 50 per cent by the tenth day."

In this series the greatest weight loss occurred during the 72 hours after delivery (Fig. 2). These infants sustained a loss which averaged 7.8 ounces, or 6.5 per cent of their birth weight. There were 14 babies who either lost no weight or gained weight without loss during their hospital stay. The hospital feeding routine is: Only glucose in water is given for the first twenty-four hours, and thereafter a standard evaporated milk formula with a carbohydrate supplement is given every four hours. Breast feeding approximates 25 per cent.
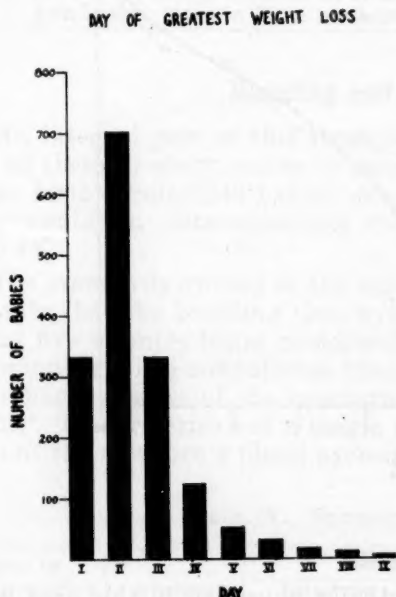
Fig. 2.
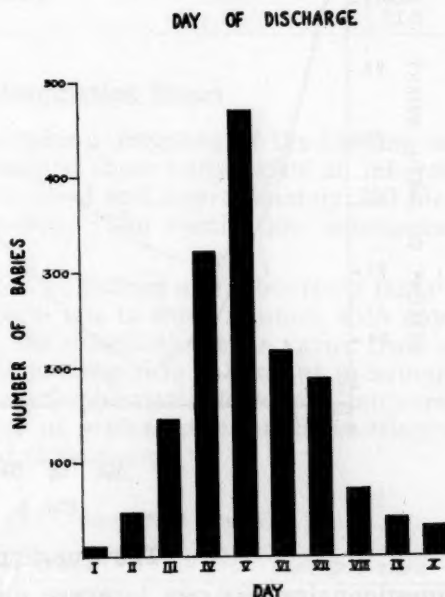
Fig. 3.

The average baby left the hospital most often on the fifth day of life (Fig. 3). At the time of discharge, the average weight was 4.2 ounces under the birth weight (3.5 per cent) but 98 per cent of all these infants were showing a progressive gain in weight at the time of discharge (Fig. 4), comparable to the series of normal infants studied by Meredith and Brown[13]; some 6.2 per cent had already equaled their birth weights and 12 per cent had surpassed them. Thus, 18 per cent of these circumcised infants equaled or bettered their birth weights at the time of discharge.

Three babies lost more than 1 pound; two of these were large infants weighing over 9 pounds with an average weight loss of 11 per cent. One infant weighed 7 pounds, 10 ounces, but contracted pneumonitis and fever, having been delivered from a contaminated mother.

The smallest babies immediately circumcised were actually **premature**, but their physicians nonetheless proceeded to circumcise them. Each of these 3 infants weighed 4 pounds, 12 ounces; their average loss was 3 ounces (3.9 per cent) during the five days they were in the hospital, and at the time of discharge 2 of these 3 had already surpassed their birth weights. Although we advocate immediate circumcision only in the full-term, normal, healthy-appearing infant there are among us some exponents of this procedure who take a more radical view. In this series, however, only 10 of the 1,480 babies studied weighed less than 5 pounds, 8 ounces at birth. It is obvious, then, that the majority agree and follow the criteria first set down by Maimonides in the twelfth century when he prohibited circumcision in any infant who demonstrated any departure from normal.[1]

WEIGHT CURVE IN FIRST TEN DAYS OF LIFE
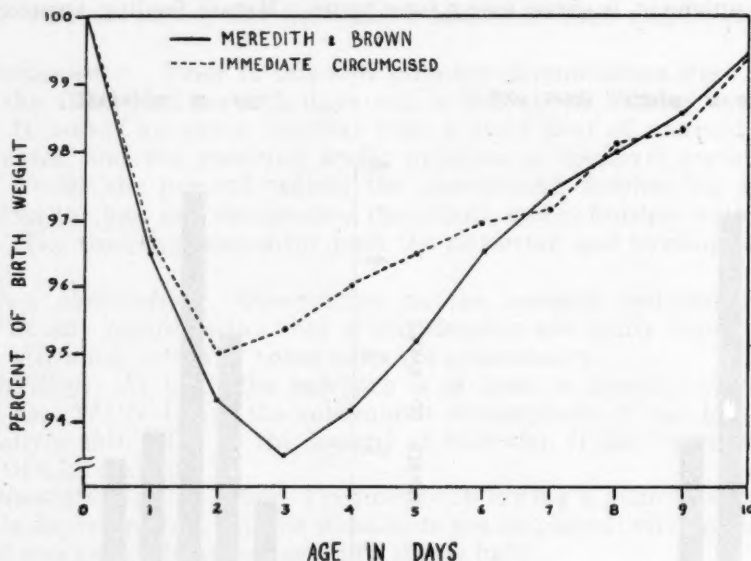
Fig. 4.

The Questionnaire

A questionnaire was sent to every practicing physician in this area who delivers babies at Akron City Hospital as well as to all pediatricians in the region who have seen the end results of this procedure. We sent out 100 of these and received 82 answers. All but two of the men were favorably inclined to immediate circumcision, and these two were not against immediate circumcision but against circumcision in general. Of the 8 pediatricians queried, 7 were in favor of immediate circumcision and had not seen any ill effects provided it was done on babies who were at term and in a good state of health.

Several reasons were listed in support of their favorable opinion, most of which we have previously mentioned; the timesaving factor and convenience were most often listed. They estimated as a group that they had performed 15,000 immediate circumcisions at this hospital, and this figure very closely approximates our own estimate; only two listed any ill effects, these being ulceration of the meatus, anemia, and undue loss of weight, but again, effects of circumcision, not of immediate circumcision.

Vitamin K was administered to expectant mothers by 16 of these physicians, 19.5 per cent, and it is interesting to note that the dosage varied from one tablet twice daily for two weeks prior to term to 10 mg. on admission to the labor room; in all, some 9 different modes of administration were listed. The results of this therapy as reflected in this study were inconclusive but in no way substantiated that of Waddell and Guerry.[11]

TABLE III. RESULTS OF QUESTIONNAIRE

QUESTION	NUMBER	PER CENT
Type of practice:		
General practice	52	63.4
Pediatrics	8	9.7
Obstetrics-gynecology	22	26.8
Favorable to immediate circumcision	80	97.5
Unfavorable to immediate circumcision	2	2.5
Have not seen complications	80	97.5
Have seen complications	2	2.5
Do not administer vitamin K to mothers	56	68.2
Administer vitamin K to mothers	16	21.9

Bleeding and Coagulation Times

An integral part of this study includes a sampling of the clotting mechanism of these newborn males to ascertain if there truly exists an inherent defect at birth. Some 348 babies were studied and approximately 700 bleeding and coagulation determinations recorded. The results are summarized in Table IV.

The standards quoted in the various pediatrics and laboratory texts[9, 10, 12, 14-18] state that the bleeding time averages one to three minutes with anything beyond five minutes being prolonged; the coagulation time varies from one to nine minutes. The coagulation time is prolonged in the infant in hemophilia, hemorrhagic disease of the newborn, erythroblastosis, leukemia, purpura, and icterus.[9] In our series not a single case of prolongation of the clotting mechanism of the newborn's blood exceeded these norms.

TABLE IV. BLEEDING AND COAGULATION TIMES

TIME OF DETERMINATION	NUMBER	BLEEDING TIME		CLOTTING TIME	
		MINUTES	SECONDS	MINUTES	SECONDS
Birth	100	1	50	3	32
Day I	105	2	20	4	25
Day II	5	2	30	4	35
Day III	81	1	45	3	40
Day IV	6	2	40	4	30
Day V	76	2	00	3	40
Day VI	7	2	35	4	50

One hundred babies were sampled at birth, and again on the third and fifth days of life, and these results are tabulated in Figs. 5 and 6. Although there were variations of insignificant amounts, the tendency was toward a slight prolongation of the bleeding and coagulation times from birth to the fifth day. Clinically, there was no bleeding at the circumcision site if a proper technique had been carried out; the babies with icterus, erythroblastosis, and purpura were not circumcised.
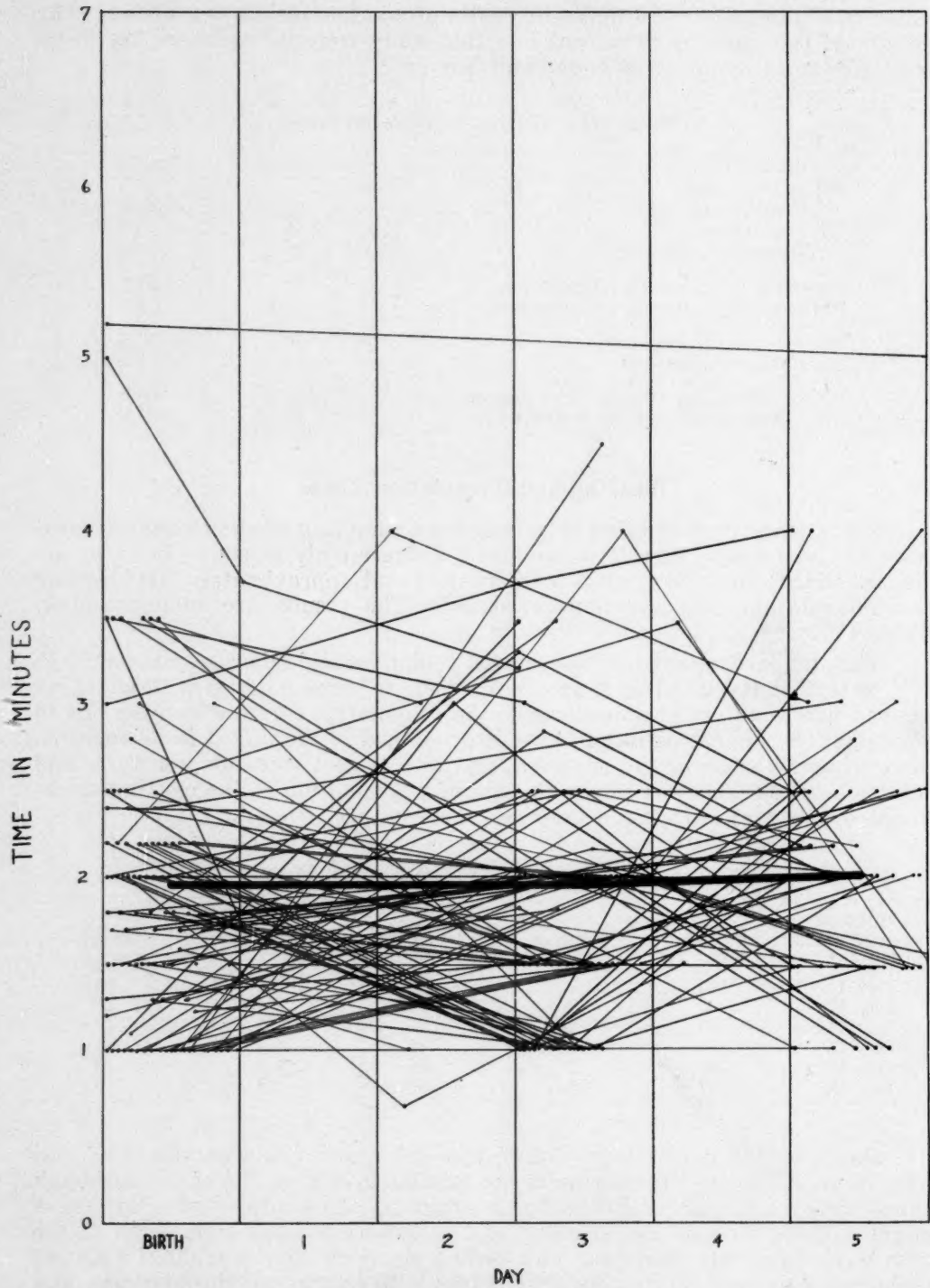
BLEEDING TIME - 100 NEWBORN MALES
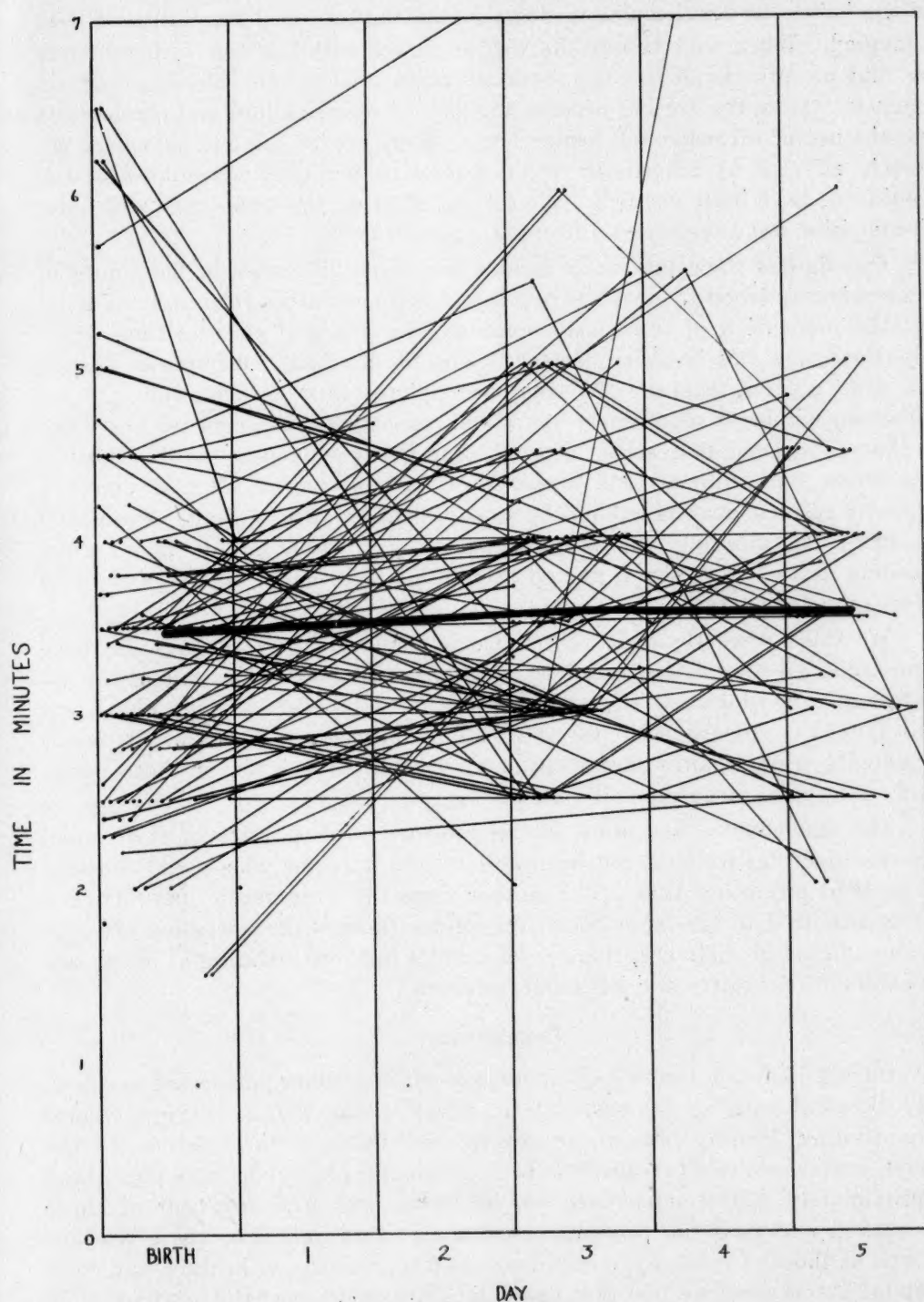

Fig. 5.

CLOTTING TIME - 100 NEWBORN MALES

Fig. 6.

Comment

This investigation of circumcision performed immediately after the birth of the baby was carried out to demonstrate the practical feasibility of such a method. When we compare the weight curves with the accepted standards we find no adverse deviation; the same holds true for the bleeding and coagulation times, the healing process, the lack of complications and particularly the absence of infection and hemorrhage. Were any of these to have been adversely affected by immediate circumcision, the practical advantages gained would not have been justified. We set out to prove its equanimity with later circumcision but have ended hinting at its superiority.

Our figures show that there is no appreciable difference in the ability of the newborn's blood to clot; whereas it was formerly taboo to circumcise without the precaution of previously obtained bleeding and clotting time determinations, now this has been discarded with no ill effect. One man in this entire area reports three deaths from hemorrhage after circumcision, yet his career encompasses some thirty years and these tragedies occurred years ago in the era of home deliveries. The bleeding that occurred in the five cases in this series was minimal and happened within two hours after the circumcision; a resident was called and by the application of very simple hemostatic measures the bleeding was stopped promptly. These infants had normal bleeding and clotting times, gained their weight normally, and showed no ill effect from the operation.

We think it worthy of more than casual mention that seven-eighths of the community's pediatricians endorsed the procedure, and all but one of the obstetrician-gynecologists. These two dissenting votes were cast by physicians who regard circumcision simply as a "useless procedure." The pediatricians repeatedly warn against circumcision of debilitated infants, or those whose mothers were Rh negative and multiparous.

The convenience and time saving afforded both physicians and nurses are considerable; we have not been able to find a doctor who would consider doing it at any other time. The mother signs the circumcision permit when she is admitted to the labor room, the doctor finishes the operation after he has completed his delivery, there is no conflict in the scheduling of cases, and no babies are forgotten and left uncircumcised.

Conclusions

During 1950 there were 1,480 immediate circumcisions performed in Akron City Hospital with no demonstrable ill effect on the weight curve, temperature, feeding, healing process, or general well-being of the infants. In the eleven years since this practice first began some 250 physicians have performed approximately 30,000 immediate circumcisions, and 97.5 per cent of those questioned endorsed the procedure without reservation. For these reasons, as well as those of economy, convenience, safety, rapidity of healing, and close hospital observation we feel that immediate circumcision of the newborn male infant might well be more universally adopted.

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ECLAMPSIA AS A CAUSE OF MATERNAL DEATH IN PHILADELPHIA*

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THE reduction in maternal mortality from year to year is likely to engender a feeling of complacency which can be rapidly dissipated by a more thoughtful study of the individual causes of death. Although the total maternal loss of 12,544 in 1935 was reduced to 4,122 in 1948, the improvement for each of the selected causes was not comparable. Deaths from infection, for instance, fell from 5,064 (40.3 per cent of the total) to 1,166 (28.0 per cent of the total), while those from eclampsia showed less change. Although there were only 1,164 deaths from eclampsia in 1948 as compared to 2,229 in 1935, the percentage of maternal deaths due to eclampsia during these years increased from 17.7 per cent to 28.3 per cent of the total. The present study was undertaken to determine the trend of mortality from eclampsia in Philadelphia for the years 1940 through 1950, in an effort to evaluate the effect of improved obstetric care and in the hope that it might indicate methods by which the number of these deaths could be further reduced.

The information was obtained by reviewing, in each fatal case of eclampsia, the summary prepared by the attending physician and submitted to the Committee on Maternal Welfare of the Philadelphia County Medical Society for study. A report was available for every recorded death from eclampsia which occurred in Philadelphia during these years; some were brief and relatively uninformative and lacked important details of observation and management of the patients, but on the whole the desired information was available. In order that no cases of eclampsia be overlooked, the information concerning each maternal death attributed to any form of toxemia during this period was reviewed. Of the total, 118 were classified as eclampsia by the Committee, by the reporting physician, or by the autopsy record, but in 23 of these sufficient evidence to support the diagnosis was lacking and consequently they were discarded from this study. The 95 selected, therefore, seemed unquestionably to have been eclampsia since all occurred during the second half of pregnancy, each had at least two of the three cardinal signs of toxemia (hypertension, edema, proteinuria) and all but 15 had convulsions. Each of the latter had definite evidence of pre-eclampsia during the prenatal period and died comatose. In some instances the patient was found in coma which may have been preceded by unobserved convulsions.

An effort was made to collect specific information in order to answer the following questions:

1. How many deaths from eclampsia occur each year in Philadelphia?
2. For what percentage of total maternal deaths do they account?
3. Is eclampsia becoming more or less important as a cause of mortality?
4. How might these deaths have been prevented?
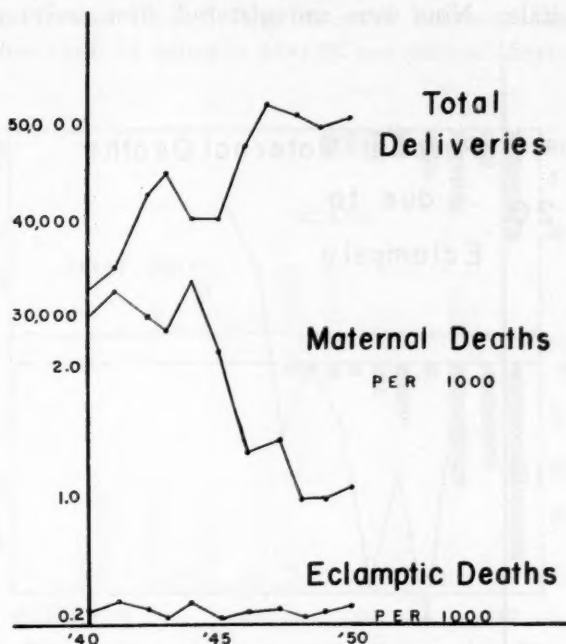
Fig. 1.—Maternal and eclamptic mortality rates.

Incidence of Mortality From Eclampsia.—During the years 1940 through 1950 the total number of deliveries in Philadelphia increased from 32,190 to 48,459, while maternal deaths were reduced 58 per cent from 74 or 2.4 per 1,000 to 48 or 1.0 per 1,000 (Fig. 1). During this same interval, 95 women died as a result of eclampsia, the number varying little from year to year. Although the actual incidence of eclampsia was undoubtedly reduced during this period, the number of deaths resulting from the condition remained relatively unchanged and therefore it assumed an increasingly important place in the final analysis. This is indicated by the fact that it accounted for only 10.8 per cent of the total maternal loss in 1940 as compared with 20.8 per cent in 1950. In addition to the maternal mortality a high fetal loss was observed. Only 30 infants were born alive; of the others, 49 were stillborn and 22 died undelivered, thus the total loss of life was 166. Since this condition appears to exert so undeniable an influence on maternal and infant death it seems important to search for factors which should have alerted the physician in time to institute measures which might have altered the results.

General Factors.—Eclampsia occurred in primigravidas in only 53 per cent of these cases, which is somewhat lower than the usual figure, but 9 (21 per cent) of the multiparas were known to have had antecedent vascular disease

making them more susceptible. Multiple pregnancy is known to be accompanied by an increased incidence of toxemia and was observed five times, more than quadruple the expected incidence.

Type and Duration of Prenatal Observation.—Since eclampsia is more commonly encountered in underprivileged groups the type of medical care as an index of the patient's means was noted. Private physicians supervised the care of 52 patients while 34 had registered in the outpatient departments of various Philadelphia hospitals. Nine were unregistered, first arriving at the hospital
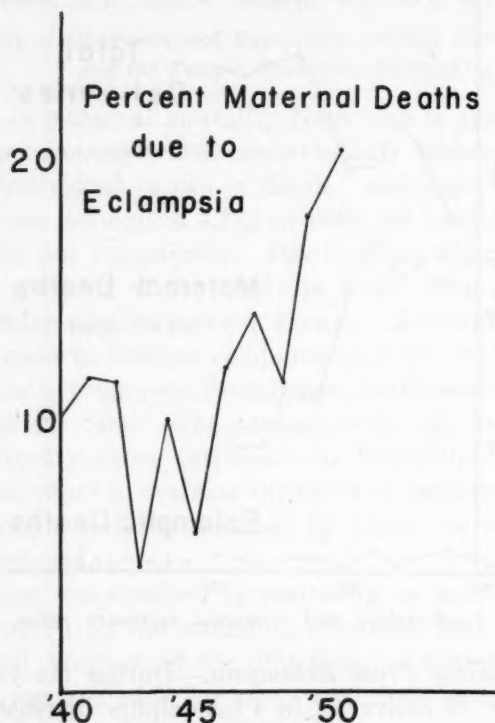
Fig. 2.—Percentage of maternal deaths due to eclampsia.

in convulsions or in coma. Since some of the patients might have registered too late to receive the utmost advantage from prenatal care, an analysis was made of the time in pregnancy at which the patient was first examined and the time at which she died of eclampsia (Fig. 3). It is obvious that in both the private patients who first consulted their physicians at an average of 12 weeks (6 to 36 weeks) of pregnancy and the ward patients who registered at an average of 20 weeks (12 to 36 weeks), the physician almost always had ample opportunity to initiate and direct a sound program for prenatal management. In 3, the summaries reported eclampsia of such a fulminating nature that premonitory evidences were entirely lacking. One, for instance, was an 18-year-old primigravida whose blood pressure ranged from 82/40 to 100/70 and in whom no abnormalities were noted at any of her three visits at 22, 24, and 27 weeks of pregnancy. Ten days after the last visit the patient was admitted to the hospital in convulsions and died of eclampsia.

Duration of Pre-eclampsia.—Since most of the patients had registered during the first half of pregnancy, it seems likely that the early evidences of toxemia should have been detected. Despite the fact that warning signs such as abnormal weight gain, edema, blood pressure elevation, and proteinuria usually were reported on summaries as having been noted during the prenatal period, 42 patients experienced the first convulsion before admittance to the hospital (Fig. 4). Under these circumstances, opportunity for adequate definitive treatment was limited, the interval between the first convulsion and death being less than 24 hours in over 60 per cent of these cases.
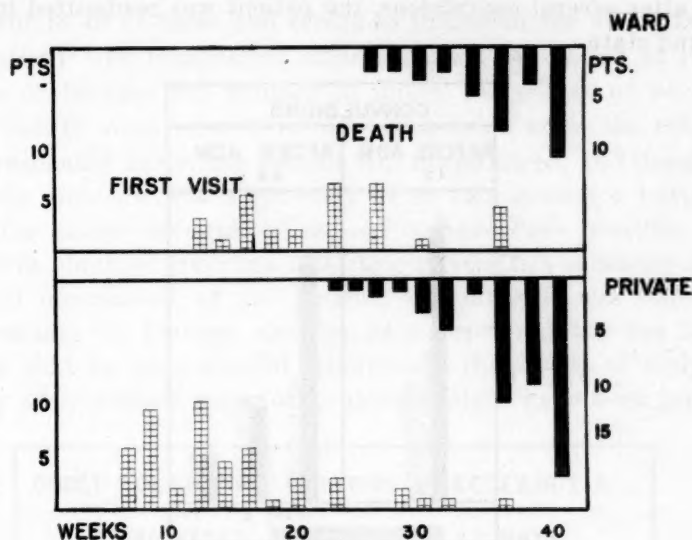
Fig. 3.—Time of registration and time of death.

Since the death rate increases so sharply if the patient is allowed to develop eclampsia and since pre-eclampsia is not at this time preventable, early recognition and systematic treatment of toxemia become the most important factors in reducing mortality. In those fatal cases in which eclampsia occurred within four weeks of term, signs of pre-eclampsia were first noted on an average of 17 days before the initial convulsion (Fig. 5). In contrast, those whose eclamptic episode occurred before the thirty-second week of pregnancy appeared to run a more rapid course since signs of pre-eclampsia obvious to the physician had been noted only 6 days previously. It is possible that the condition had been present but unrecognized for longer periods of time in some of these patients, particularly if the disease occurred relatively early in pregnancy at a time when the intervals between visits were longer than during the last few weeks.

Office Therapy.—An attempt was made to evaluate treatment before admission to the hospital and in only 27 instances was therapy considered to have been adequate. Adequacy of treatment was assessed on an exceedingly liberal basis since almost any reasonable attempt to correct the changes was thus classified. If the condition was ignored by either the patient or the

physician, if no treatment was suggested, or if contraindicated measures were instituted, the program was considered to have been inadequate. In one of the summaries, for instance, a 25-year-old para 0, gravida i, was reported to have had a normal prenatal course until the thirty-seventh week of pregnancy at which time albuminuria and hypertension were observed. On a visit at the thirty-eighth week it was noted that these findings were "higher than after one week's rest in bed at home." Medical induction of labor was attempted at home and three days later the patient was admitted to the hospital in "mild labor" but contractions ceased and she was discharged the following day. Five days later, after several convulsions, the patient was readmitted to the hospital in a moribund state.
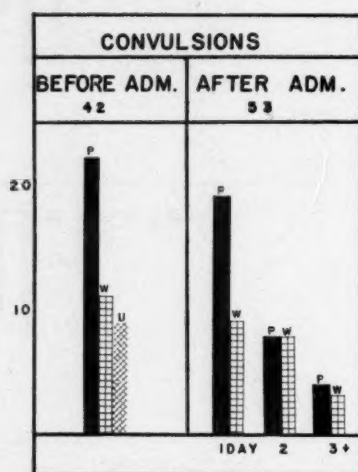
Fig. 4.—Time of onset of convulsions.

Hospital Therapy.—Treatment in the hospital ordinarily consisted of emergency therapy for the convulsing patient and consequently was for the most part heroic but terminal. In 7, death occurred before any form of treatment could be instituted. As in the prenatal period there was a marked variation in the type of treatment but more patients (55) were considered to have been adequately managed after hospitalization than before. In many instances, however, even though the patient was admitted before the onset of convulsions, treatment was either inadequate or harmful. In most cases minimal sedation was prescribed, no efforts were made to correct the disturbance of water balance and the pregnancy was allowed to continue despite obvious evidence of progression of the toxemia. Of the 32 hospitalized patients who were inadequately managed, the treatment itself was thought to have contributed to death in six. In one of these the patient had been hospitalized for six days with severe pre-eclampsia. Medical induction and frequent stimulation produced contractions which continued irregularly for three days before convulsions and death occurred. Not until the uterus was opened to perform postmortem cesarean section was the diagnosis of transverse lie made. In another patient a well-timed surgical induction was carried out for severe

pre-eclampsia but marked cephalopelvic disproportion was unrecognized and labor continued for 48 hours. An attempted forceps delivery failed and was followed by cesarean section. The first convulsion occurred during the operation. Others in this group include those in whom accouchement forcé was the sole attempt to solve the problem and one in whom the infusion of large amounts of sodium-containing solutions increased the toxic signs.

Preventability.—From the information available at least 75 per cent of these deaths were thought to have been preventable. In 48 the responsibility was regarded as primarily the physician's, inadequate prenatal care being the principal factor in 15 of these and errors in judgment the major factor in 33. In 23 the patient was responsible either because she failed to register for prenatal care or because she refused to follow the advice of her physician. Twenty-four deaths were considered nonpreventable since the condition was recognized reasonably early, the patient was hospitalized, and despite therapy died. In 3 the toxemia was apparently of so fulminating a nature that no opportunity for earlier recognition seemed to have been possible. Since the information was obtained from the attending physician's summary rather than from firsthand observation of the patient, and since it was impossible adequately to evaluate the therapy, decision as to preventability has been liberal. It is probable that by more careful attention to the details of early diagnosis and adequacy of treatment many other deaths might have been prevented.

ONSET ECLAMPSIA	DURATION PREECLAMPSIA
3 7-40 WEEKS	1 7 DAYS
3 3-3 6	1 0
3 2- OR LESS	6

Fig. 5.—Duration of pre-eclampsia.

Comment

During the years 1940 to 1951 eclampsia has played an increasingly important role in maternal mortality in Philadelphia, since the reduction of deaths from this condition has not decreased at the same rate as deaths from other causes. An analysis of the reports of these deaths indicates that at least 75 per cent were preventable, since all but 9 of the patients had been under medical supervision and had registered sufficiently early in pregnancy so that progression from mild pre-eclampsia to eclampsia was observed. Despite the fact that in only three patients were there no recorded evidences of pre-eclampsia, 42 experienced the initial convulsion before admittance to the hospital. This suggests that the physicians were unimpressed with the seriousness of the progressive signs of pre-eclampsia which they noted and recorded. More careful management might frequently have altered the end result. Since the exact etiological factor responsible for toxemia of pregnancy is unknown

it cannot yet be prevented. It can, however, be recognized early. Recognition of the seriousness of mild pre-eclampsia, its active treatment, and termination of pregnancy if it does not respond will prevent eclampsia with its high mortality. This, at the moment, offers the best chance for reducing deaths from toxemia.

Any program for the prevention of eclampsia must concern itself primarily with prenatal care. A diet adequate in protein and low in salt with a caloric content sufficient to permit only a normal weight gain should be prescribed for each patient. Since the initial evidence of pre-eclampsia usually is an abnormal gain in weight, sudden increases, even though the blood pressure is within normal limits, must be viewed with suspicion. Continued weight gain or the appearance of edema despite repeated instruction suggests that the patient is ignoring the dietary advice or that the condition is not responding to therapy and more drastic measures must be instituted. Although hypertension is an important sign of pre-eclampsia it usually appears after an abnormal weight gain becomes evident. If only those patients whose blood pressures are elevated above 140/90 are treated, many will be given their first therapy after the onset of convulsions. Blood pressure is within normal limits early in the course of the disease, hence one must be concerned over any rise even though it is still within the limits of normal. This is particularly true if it is associated with an unusual gain in weight. If early pre-eclampsia is suspected active therapy directed toward elimination of excessive fluid and prevention of progression of the toxemia must be instituted at once. It is necessary to re-evaluate each patient in 2 or 3 days to determine the effect of treatment. This is particularly true if the initial signs appear around the thirtieth week since the course of pre-eclampsia is more fulminating then than later in pregnancy. Although the fluid retention and weight gain can often be corrected by diet, the blood pressure may remain elevated. Should the hypertension increase, or symptoms appear, continued observation is hazardous.

Failure to reverse or at least stabilize the signs by home or office treatment constitutes an indication for hospitalization in order that the patient can be more thoroughly studied and more actively treated. Essentials in the hospital management of pre-eclampsia include controlled diet, stimulation of urinary output and mobilization of the retained extravascular fluid, control of hypertension with bed rest and sedation, and delivery if termination of pregnancy becomes necessary. During the period of medical management, observation includes frequent determinations of blood pressure, daily weight, the daily calculation of fluid intake and output, the daily determination of the total urinary protein excretion, examination of the ocular fundi, and frequent determinations of hematocrit for evidence of hemoconcentration.

The patient with severe pre-eclampsia who is admitted to the hospital with marked edema, hypertension, and proteinuria may have oliguria and symptoms such as headache, visual disturbances, or epigastric pain. A period of intensive medical management directed toward reducing cerebral edema and irritability, promoting urinary output, and reducing edema should precede

any attempt at delivery. Necessary studies include those listed for the less severe toxemia. During the period devoted to medical control constant observation is necessary to detect failure to respond. If the weight increases, urinary output remains low, symptoms fail to regress, and the blood pressure rises despite therapy, termination of pregnancy before convulsions ensue is necessary. In those who respond favorably, termination of pregnancy must be considered after the toxemia has been stabilized for 24 to 48 hours. Procrastination may permit a return of all the symptoms and favors the progression to eclampsia. Vaginal delivery is preferable if the cervix is ripe and labor can be induced. Cesarean section should be reserved for the small percentage of patients in whom there is an obstetric indication and for those who must be delivered despite an unprepared cervix.

The treatment of active eclampsia is of necessity accompanied by a high mortality rate while that for pre-eclampsia is low. If pre-eclampsia is detected and painstakingly treated its progression may be prevented. It is important to remember that all patients who develop eclampsia have gone through a stage of mild pre-eclampsia which may be rapid or prolonged depending upon factors not well understood at this time. The recognition of the seriousness of mild pre-eclampsia and its active treatment should prevent most cases of eclampsia with its attendant high mortality rate. A careful program of frequent examination and office therapy directed toward reversing the abnormal changes will control some. Admittance to the hospital for closer observation and more active treatment is indicated for those who fail to respond. Delivery, if the process progresses despite active therapy or after severe pre-eclampsia is controlled by medical therapy, will keep both maternal and fetal mortality rates at a minimum.

Discussion

DR. PHILIP F. WILLIAMS.—I was interested to hear Dr. Carrington's paper on the mortality from eclampsia. This makes the fourth time that a survey of eclampsia has been made since the Committee on Maternal Welfare was formed. I am rather sorry that some of the conclusions drawn in the earlier papers are still being neglected. One has to feel that there has been some reduction in the number of deaths from toxemia in the city of Philadelphia, because I am sure that with 48,000 deliveries there must have been many mild and severe pre-eclampsia cases that were treated successfully. If we knew how many pre-eclamptic patients were admitted to the hospitals during the past ten years we would find that we have improved more than indicated in the treatment of these cases.

That maternal mortality from eclampsia has jumped from 10 per cent in 1940 to 20 per cent in 1950 is due in large part to medical advances, such as the new drugs to control infections, and reductions in other categories brought about by blood banks. These play a part in the fact that eclampsia stands rather high, just as cardiac and cancer deaths have moved up over typhoid fever and tuberculosis in recent years. I was interested by the fact that Dr. Carrington showed figures on stillbirths and neonatal deaths. Dr. Reichstein and Dr. Rose have done a good job on this. We have to look at the whole picture. Whether the mother or the fetus, or both, die, the total has to be considered.

Special attention should be placed on family history of pregnant women of high blood pressure, heart disease, renal syndrome, etc. Special notations should be made when there is a history of such deaths in the family.

Dr. Carrington emphasized the importance of early prenatal care and looking for signs of pre-eclampsia and giving prompt treatment. I question the efficacy of trying to treat

the toxemia at home or in the office. I do not believe pre-eclampsia should be so treated. If the woman has enough signs to worry about she should be placed in the hospital. Since we have seen figures about the accuracy of diagnosis and the treatment of such patients, I think it is the duty of the attending chiefs in the hospitals where a good many doctors come and deliver women to see that there are accuracy in diagnosis and well-grounded rules, outlining a definite type of treatment to be followed in pre-eclampsia and eclampsia.

One test I regard important is examination of the eye grounds in these women. Often you find eclampsia superimposed on an old renal condition, and I think a great deal of help is received from ophthalmologic examination of this type. I think we should drop the term "preventability" in referring to the cause of death, and simply give the primary avoidable factor.

One thing that leads to an increase in the number of women who died from eclampsia is the reluctance to terminate the pregnancy. Don't say, "Let's carry the woman until she has a viable child." Dr. Carrington has stated that when women have recovered from severe pre-eclampsia the pregnancies should be terminated when the condition is stabilized. In early days we had many women come into the hospital whose condition was stabilized and they went home. There was no follow-up of any kind and two or three weeks later many returned in convulsions and died.

Four questions were proposed. The first two were answered satisfactorily. The third is whether eclampsia has become more or less important as a cause of death in this city. I think it is more important. The last question: What can be done about this situation? Just this, patients must have more education about seeking earlier prenatal care and they must have better medical and hospital care.

DR. J. EDWARD LYNCH.—There are still many physicians, some of whom are obstetricians, who do not sufficiently emphasize in their prenatal care the importance of proper nutritional standards—sufficient protein, minerals, fluid control, salt restriction, etc. They allow patients to gain excessive amounts of weight. I argue with many patients about their gain in weight and often they tell me they have been previously cared for by well-thought-of obstetricians and they were allowed to gain 40 to 50 pounds. I think it is important to emphasize that excessive weight gain in pregnancy is dangerous. Taking into consideration the increase in the size of the uterus, amniotic fluid, etc., the normal 7 pound baby represents about 14 pounds' weight gain. If we remember this, we will emphasize the dangers to patients and check them carefully. I wonder whether Dr. Willson and Dr. Carrington have any figures on weight gain in these patients who have died further to emphasize weight gain and proper diet in pregnancy.

DR. LEON REIDENBERG.—I wondered whether you had figures on blood chemistry studies in these cases and, if so, what the uric acid and carbon dioxide combining power were in the study of such patients.

DR. GLENN S. DICKSON.—In those cases of difficult weight reduction, is there any contraindication to the use of the weight-reducing drugs such as Dexedrine Sulfate?

DR. CARRINGTON (Closing).—As regards the statistics on the total weight gain, actual figures were not available in most of these summaries. However, statement of the fact that the gain was excessive and frequently sudden was rather consistently noted. Most of the less routinely used laboratory studies such as the carbon dioxide combining power and blood uric acid studies were generally not mentioned. While the straight blood uric acid levels without clearance studies are elevated in advanced pre-eclampsia, it is frequently a late sign and therefore less helpful than methods previously mentioned in determining the status of the patient.

There is no contraindication to the use of Dexedrine and similar drugs used to control weight. These may be of use in the patient whose caloric intake has been over the requirements of pregnancy but one should remember that it is the fluid retention rather than the fat which is responsible for the disturbed physiology characterizing pre-eclampsia. The major efforts, therefore, should be directed toward the reversal of this abnormality.

TREATMENT OF POSTSPINAL HEADACHE WITH BUCCAL TABLETS OF DESOXYCORTICOSTERONE ACETATE

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ONE of the few deterrents to the use of saddle block anesthesia in obstetrics is the occurrence of postspinal puncture headaches. Many investigators have attempted to determine the etiology, and the consensus is that it results from leakage of spinal fluid following dural puncture. It has been postulated that the loss of the "water pad" of the brain permits the brain to rest on bone, with irritation of dural fibers of the trigeminal and occipital nerves,[7] or causes venous congestion due to pressure on the basilar venous sinuses.[10]

Alpers[1] has stated that spinal puncture resulted in a marked fall in spinal fluid pressure and that leakage through the spinal puncture wound maintained the low pressure. Nelson[11] reported a fivefold decrease in spinal pressure at the time of puncture, thus supporting Alper's view. Baruch[6] concluded that there was leakage through punctured dura from the following experiment: He injected 3 c.c. of 2 per cent indigo carmine into the subarachnoid space and was unable to demonstrate the dye in the urine in 63 minutes when the needle remained in place; whereas, when the needle was removed, indigo carmine was found in the urine in eight minutes.

Some authorities ascribe the headaches to poor technique. A small-bore needle is apparently important, since Green,[5] using suspended spinal cords injected with water, found that small needles, cleanly introduced, merely separated the fibers and produced no leakage. Large irregular holes were produced when large-bore needles were used. Kennedy[9] reproduced these results on a living calf after laminectomy of the lower thoracic vertebrae.

Methods

Our technique was designed to lower the incidence of postspinal headache as much as possible. Although the 300 cases reported here involved 14 operators, including 10 rotating interns, the following procedure was standardized: We used a No. 22 sharp spinal needle with a short bevel. The needle and syringe were rinsed thoroughly with sterile distilled water and the needle was inserted with the bevel parallel to the long axis of the body. One c.c. Nupercaine hydrochloride, 1 part to 400, was introduced slowly with the bevel pointing caudad. The needle was left in situ for approximately 15 seconds and then removed carefully and gently to avoid any trauma. The patient was kept in a sitting position for 30 seconds after introduction of the anesthetic agent, then placed in a supine position with head slightly elevated.

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Results

Of the 300 patients who received saddle block anesthesia at St. Louis County Hospital during the period of this study, 70 developed what was considered postspinal headache. In order to attribute a headache to saddle block, we required that it must be almost completely relieved when the patient was recumbent and accentuated by the erect position. The headaches were usually occipital but might be generalized. Occasionally the patients complained of stiff neck or pain across the shoulders; infrequently of nausea or vomiting, or both.

The incidence of postspinal headache in our series, 23.3 per cent, corresponded closely to that of Andros, Priddle, and Bethea,[4] who reported an incidence of 20.3 per cent in 182 consecutive patients anesthetized with saddle block Metycaine (benzoxy-γ-[2-methylpiperidino]-propane hydrochloride). The typical time of onset of headache was 36 to 72 hours post partum. There was a higher percentage of primiparas in our headache group (38.5 per cent) than in our total group (28 per cent) and 28.5 per cent of the headache group had a concomitant complication (anemia, infection, etc.). However, with respect to such other features as age, duration of procedure, operation, amount of drug used, infections, and their effect on the incidence of postpuncture headache, no significant correlations were found in over 15,000 cases analyzed by Asbell.[5]

Thirty-five of the 70 headache patients were treated by conventional methods such as caffeine with sodium benzoate and other stimulants, intravenous fluids, ergot derivatives, vitamins, salicylates, and codeine. This treatment was, in the main, unsuccessful. The remaining 35 patients were treated with buccal tablets of desoxycorticosterone acetate (Cortate).

We used desoxycorticosterone acetate (DCA) on the basis of a report by Asbell.[5] He administered, by intramuscular injection, 5 mg. DCA dissolved in 1 c.c. sesame oil daily, usually for three days, to his patients with postspinal headache and achieved complete relief in 92 per cent of cases. Our buccal tablets were in a polyethylene glycol wax base each containing 2 mg. of the hormone. The efficacy of DCA in this form has been shown to be somewhat less than 2:1 when compared to DCA given intramuscularly in the maintenance of 14 known Addisonian patients.[2, 3]

Intramuscular DCA, 5 mg. every eight hours, completely relieved 10 patients who complained of headache as well as nausea and vomiting following radiation therapy, according to a recent report,[8] and we first administered the 2 mg. buccal tablets every eight hours. An occasional patient, however, would complain of a recurrence of the headache about six hours following medication so we changed the dosage schedule to one buccal tablet every four to six hours as necessary.

Since these headaches are believed to be due to low spinal fluid pressure, perhaps the action of DCA is to elevate spinal fluid pressure by raising the concentration of serum sodium and thereby increasing extracellular fluid. Other possibilities are the "pressor" principle of DCA or a proposed reciprocal effect via the anterior pituitary causing increased production of fluid by the choroid plexus.[5]

Early ambulation was ordered in all of the uncomplicated cases. Soon after the use of DCA was initiated, it was observed that usually in 30 to 60 minutes patients were relieved of the headache and were able to be up and about the ward. Relief persisted as long as 24 hours in a few cases. The dosage was repeated for as many days as necessary if the patient complained of return of headache. One or two days of treatment was the usual course, but several patients required additional doses on the third and fourth days.

No side actions to the use of the hormone were noted, and the results were very gratifying. Thirty of the 35 patients (86 per cent) obtained complete relief, and three (8.6 per cent) were partially relieved. Two patients not relieved by DCA were relieved by codeine.

Summary

The etiology of postspinal headache is discussed, the consensus being that postspinal puncture headaches are due to leakage of spinal fluid with fall in spinal fluid pressure.

Treatment with caffeine and other stimulants, ergot derivatives, fluids, vitamins, salicylates, and codeine for the relief of these headaches has been consistently ineffective in our institution.

Thirty-three of 35 patients obtained relief from postspinal headache when given buccal tablets of desoxycorticosterone acetate. Thirty had complete and prompt relief for a period of one to four days after the drug was administered with no recurrence thereafter. No side effects were noted.

The desoxycorticosterone acetate used in these studies was supplied by the Schering Corporation, Bloomfield, N. J., as Cortate Buccal Tablets.

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A THIRTEEN-DAY NORMAL HUMAN EMBRYO SHOWING EARLY VILLOUS AND YOLK-SAC DEVELOPMENT

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THE finding of a human embryo during routine uterine curettage is both fortunate and unusual, particularly in view of the fact that no unusual precautions for fixation, cutting, and staining are usually taken. Hertig and Rock[1] over a ten-year period at the Free Hospital for Women discovered 28 early conceptuses in uteri removed therapeutically for a variety of reasons but with the specific intention of ovum search. All were younger than 16 days and were obtained from a study group of 136 cases. In this project, however, extreme care and planning were utilized both in the timing of the operative procedure and in the pathologic preparation of the specimens. None were obtained by uterine curettage.

The ages of the conceptuses varied from a 4½ day blastula of about 60 cells, measuring 130 microns, found floating freely in the uterine cavity to a 16 day early villous specimen interstitially implanted and measuring 2.2 by 2.35 by 3.75 mm. Of the 28 early pregnancies obtained, 12 were abnormal and these have subsequently been reported as a series of potentially abortive ova.

Wilson,[2a] in discussing the latter presentation, reported an 11 to 12 day normal human ovum which had been obtained accidentally during an endometrial biopsy. Wilson[2b] had previously described a 16 day human ovum obtained by curettage in 1945 and in the same year Marchetti[3] discovered a previllous ovum in routine curettings. Ramsey[4] described in 1938 the so-called "Yale Embryo," a specimen obtained during a routine autopsy, and Scipiades[5] noted a similar ovum detected in uterine curettings in the same year.

The following case report is deemed of interest because of its rarity, the apparent normality of the ovum, and the age of the conceptus—a stage somewhat younger than that of the 13½ day villous ovum of Heuser, Rock, and Hertig.[6]

Clinical History.—

The patient (Kings County Hospital Unit No. 3610) was a 30-year-old obese unmarried Negro woman, para ii-o-i-ii. She was admitted from the outpatient department on Jan. 20, 1952, with a chief complaint of low back pain of two years' duration. In addition, a routine cervical biopsy taken in the clinic had revealed intraepithelial carcinoma and the patient was admitted primarily for knife biopsies of the cervix. The family history revealed paternal diabetes. The patient had had an appendectomy in 1939 which was uncomplicated. She had noticed intolerance to fatty foods, occasional right upper quadrant pain, and dark urine for 6 months prior to admission. Catamenia began at age 14 and lasted three to four days with a 28 day cycle. The last normal menstrual period began on Dec. 24, 1951, and the previous

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menstrual period on Nov. 27, 1951. A history of intercourse in the late evening of January 8 was elicited (sixteenth day of the cycle). No other intercourse occurred prior to hospital admission.

Physical examination revealed an obese Negro woman in no distress. The blood pressure was 110/70 and the general physical examination was negative. Pelvic examination revealed normal external genitals, a marital introitus with moderate cystorectocele, Skene's and Bartholins glands were negative. The vagina was normal. The cervix was firm, mobile, and nontender and the uterus slightly enlarged, anterior, firm, and mobile. The adnexa were negative. Speculum examination revealed the cervix to be pink and apparently well epithelized. A recent biopsy site at 12 o'clock was visible. A Schiller test revealed nonstaining areas at 7 and 11 o'clock.

On Jan. 21, 1952, at 9 P.M., deep knife biopsies were taken through the Schiller-positive areas and also at 12 and 6 o'clock. An endocervical and endometrial curettage was performed under cyclopropane anesthesia. Approximately 4 c.c. of soft, gray-red endometrial tissue was removed. It did not seem grossly unusual.

The specimen was fixed in 10 per cent neutral formalin, processed through a technicon, and embedded in paraffin. It was sectioned at 10 microns and stained with hematoxylin and eosin.

Fig. 1.—Implantation site, showing the relation of the ovum to uterine tissues. Note chorionic cavity, primitive unbranched villi, and lacunar (intervillous) spaces. Several large, thin-walled endometrial sinusoids may be seen immediately adjacent. (Hematoxylin and eosin. ×35.)

Description of Specimen (S-52-610)

This specimen was first processed through the Department of Pathology and one slide prepared at 10 microns. The tissue consisted of a group of fragments of curetted endometrium which were imbedded together in a block of paraffin 4 mm. in thickness. The original slide consisted of four larger fragments of endometrium approximately 3 by 2 mm., together with several smaller fragments. The fragments were not oriented before cutting. Only the first slide contained the ovum and germ disc illustrated and described herein. However, before the ovum had been discovered, the block was recut for additional sections

and, in so doing, the area of the germ disc was inadvertently discarded. Subsequent recutting of the block into 65 additional slides revealed 48 which contained the chorionic cavity but in none was the germ disc or extracelomic membrane evident.

The implanted ovum was situated on a small endometrial fragment 2 by 4 mm. in greatest diameters. The site of implantation produced a semispherical elevation above the surface endometrial epithelium which measured 1.4 mm. in diameter at the base and 1.1 mm. in height.

The surface endometrial epithelium had not yet covered the ovum and its distal or free end was made up of several layers of syncytiotrophoblastic cells and cytotrophoblastic columns. Numerous lacunar spaces were here well formed, lined by syncytium, and occasional groups of erythrocytes were seen in several of these primitive intervillous spaces.

Uterine glands subjacent to the ovum appeared not to have been modified by implantation. They were regular, with clear lumina and pale, vacuolated lining cells. Deeper in the endometrium the glandular lining cells were just beginning to discharge glycogen into the lumina. For the most part they were elongated and tortuous but not as yet serrated.

Immediately adjacent to the implantation site were several endothelium-lined sinusoids. One contained a clump of erythrocytes and monocytes but congestion was not present. One sinusoid was partially surrounded by a layer of syncytiotrophoblastic cells but "tapping" or intravascular syncytium was not evident.

Throughout most of the endometrial fragments the stroma showed a well-developed decidual reaction, particularly surrounding the arterioles, and focally sheets of these cells were evident under the surface epithelium. There were no inflammatory cells present in these decidual sheets. In other areas there was marked stromal edema and interstitial stromal hemorrhage.

Large, irregular, and stellate-shaped cells with deep basophilic nuclei and purplish cytoplasm were seen scattered in the stroma adjacent to the ovum. These syncytial wandering cells had focally formed "giant cells" and had lined up around an occasional blood vessel.

Chorion.—

The chorionic cavity was somewhat pyramidal in shape and measured 0.6 mm. by 0.81 mm. The embryonic surface of the cavity was completely lined by cytotrophoblast and columns of cytotrophoblast were seen pushing out and everting overlying sheets of syncytium into the lacunar spaces, thus forming the primitive villus. These villous buds contained neither mesoblastic tissue nor vessels and approximated 0.20 mm. in length. The total amount of syncytiotrophoblast present at this stage almost equaled the amount of cytotrophoblast. The entire chorionic cavity was surrounded by irregular lacunar spaces and interposed primitive villi.

The chorionic sac contained loosely scattered filamentous and pyramid-shaped cells in a spider-web matrix. Aggregates of erythrocytes were also seen. This tissue, as in the 13½ day Heuser-Rock-Hertig embryo, was more abundant between the amnion and chorionic wall and would later condense further to form the body stalk. It has previously been shown[7] that these extraembryonic mesoblastic cells originate in situ by delamination from the surrounding cytotrophoblast. The true chorion is thus composed of two layers, an inner mesoblastic and an outer trophoblastic.

No true vesicles per se were seen, in the peripheral part of the chorionic cavity and the exocelomic membrane could not be identified. Hertig[8] has stated that this evanescent structure reaches its peak of development during the twelfth day and rapidly declines thereafter. A remnant of this structure is still seen, however, in the 13½ day ovum previously mentioned.[6] It is entirely possible that it was still present in our embryo deeper in the paraffin block but because much of the block was partially destroyed in preparing the single section, the exocelomic vesicle may have been by-passed.

The Embryo.—

The germ disc was irregularly elliptical in outline, measuring 0.05 mm. by 0.27 mm. Its thickness was uniform and it was composed of darkly staining, somewhat cuboidal cells

arranged in a bilaminar and occasionally trilaminar pattern. The primitive streak was evident as a median downgrowth of clumps of cells on the ventral surface of the disc. A few cells arranged loosely beneath the ectoderm and lateral to the primitive streak comprised the embryonic mesoderm.

Amnion.—

The amniotic cavity was situated on the dorsal aspect of the germ disc, toward the implantation area and was hemispherical in outline. It measured 0.22 mm. by 0.073 mm. and was bounded by a single layer of delicate stellate cells, the amniotic membrane. The amnion was suspended by a gossamer network of cuboidal cells, extraembryonic mesoblastic connective tissue, attaching it to the inner margin of the cytotrophoblast. The amnion, originating as it does about the eighth day from two sources, that is, by delamination of the cytotrophoblast and splitting off of ectodermal cells from the germ disc, has been described[6] as being made up of an inner lining of squamous cells and an outer coat of mesoblast. In our specimen this outer coat was well demonstrated whereas only a few inner cells were identified.
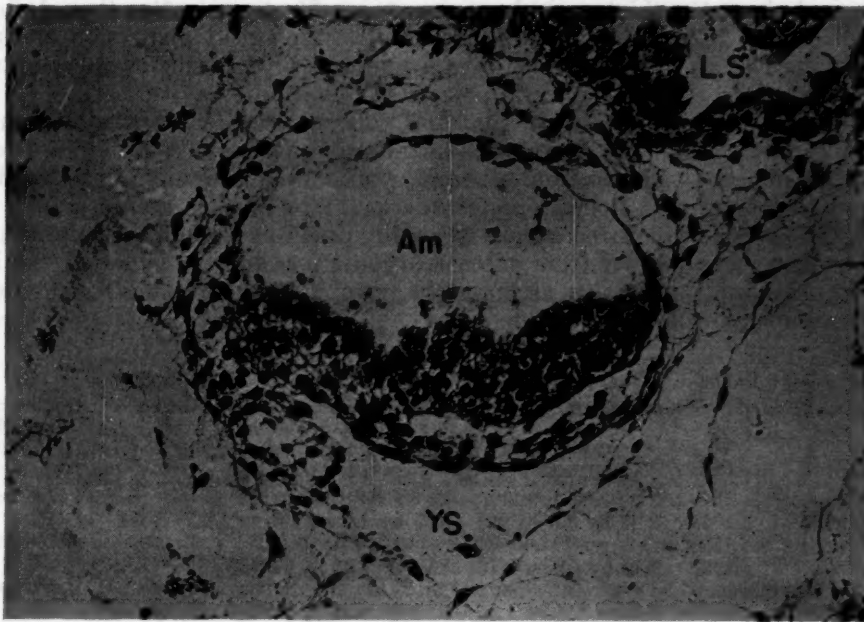
Fig. 2.—Embryo, yolk sac, and amnion seen in higher magnification. At turned-up margins of bilaminar ectodermal plate there is a transition to thin squamous cells of the amnion (AM). Cytotrophoblast of chorion visible in right upper quadrant with syncytium-lined lacunar space (L.S.). Foamy nature of gut endoderm and endodermal cells lining yolk sac visible (YS). (Hematoxylin eosin. ×250.)

Yolk Sac and Gut Endoderm.—

The yolk sac was roughly triangular in shape and measured 0.17 mm. by 0.045 mm. in greatest diameters. The wall was not as yet bilaminar throughout its entire extent as described in later embryos of 13½ days and 16½ days, and was made up of a single layer of mesoblastic cells. At one edge of the sac cavity there was an accumulation of larger, more compact cells—the primitive gut endoderm—growing into the yolk sac, forming its inner lining.

The gut endoderm was seen ventral to the germ disc and was composed of moderately large, vesicu'ar cells, many of which were surrounded by foamy, vacuolated spaces. This particular feature of primitive gut endodermal cells has been frequently observed in previously described specimens.[9, 10, 11, 12] A double layer of endodermal cells formed the dorsal boundary of the yolk-sac cavity.

Comment

The exact time, origin, and method of development of the yolk sac in the human embryo are of considerable interest and remain, at the present time, controversial. It is known that it is not present in the 12 day specimen of Hertig and Rock[9] but is a definite structure in the 13½ day embryo.[6] This would place its development as beginning sometime during the thirteenth day. Previous observations in the macaque by Heuser and Streeter[13] have shown the yolk sac to form during the twelfth day when the exocelomic membrane is still well developed. The embryo described herein would be, on the basis of single sexual contact and correlation between its occurrence and the time of uterine curettage, about 13 complete days of age.

It has not been definitely ascertained whether the yolk sac in the human being is formed, in part, by collapse of the exocelomic membrane (Heuser's membrane) or whether it forms autonomously. This evanescent, mesothelium-like membrane, first described by Heuser in 1932,[14] lines the chorionic cavity during the ninth to the thirteenth days of development. Its function is unknown and about the thirteenth day it bursts, as Hertig says,[8] as though it were a tiny balloon. No specimens depicting this physiological dispersion are available although in an ovum of 13½ days a remnant of this membrane is noted as a small vesicle in the abembryonic pole of the chorionic cavity.

It is the opinion of Hertig[8] that the yolk sac represents a new structure entirely separate from the exocelomic membrane and for a complete and excellent discussion and illustration of early yolk-sac development, the reader is referred to Hertig and Rock's[9] paper on the 11 to 12 day human ovum.

In the specimen pictured herein it would appear as though the outer surface of the yolk sac has formed from extraembryonic mesoblastic cells and the inner layer is delaminating in situ at one pole from gut endoderm. No relation to exocelomic membrane could be identified.

TABLE I. DIMENSIONS OF OVA OF GROUP VI IN MILLIMETERS

AUTHOR	YEAR	CHORION EXTERNAL	CHORION INTERNAL	GERM DISC	LENGTH OF VILLI
Peters	1899	—	1.6 by 0.8 by 0.9	—	—
von Möllendorff	1921	2.25 by 2.0 by 2.5	1.15 by 1.0 by 1.5	—	—
Fetzer	1930	—	—	—	—
Ramsey	1938	2.75 by 1.9 by 0.76	2.17 by 1.38 by 0.38	0.15	—
Edwards, Jones, and Brewer	1938	3.6 by 3.0 by 1.9	1.85 by 1.71 by 1.01	0.209 by 0.177	0.27
Heuser, Rock, and Hertig	1945	1.4 by 1.9 by 2.6	0.8 by 1.1 by 1.3	0.04 by 0.22 by 0.258	0.25
Wilson	1945	2.3 by 2.2 by 2.0	1.75 by 1.3 by 1.0	0.313 by 0.22	—
Kistner*	1952	1.0 by 1.3	0.6 by 0.81	0.05 by 0.27	0.20

*Measurements in only one plane.

In 1942 Streeter[15] outlined a classification of developmental groups of embryos (about 25 in number) to encompass the first 7 weeks of embryonic life. Chief interest has centered in the first eight groups, that is, from fertilization to the appearance of the first pair of somites. Briefly, they are: (1) one-celled stage; (2) segmenting egg; (3) free blastocyst; (4) implanting ovum; (5) ovum implanted, but avillous; (6) primitive villi, distinct yolk sac; (7) branching villi, axis of germ disc defined; (8) Hensen's node, primitive groove.

The ovum described in this report may, therefore, be placed in Group 6. Other eggs of this group previously described include the 13½ day specimen of Heuser, Rock, and Hertig,[6] Peters (1899),[16] Edwards-Jones-Brewer (1938),[17] von Möllendorff (1921),[18] and Fetzer (1930).[19] Chronologically, this ovum

appears slightly younger than the 13½ day specimen noted above and seems to present an earlier phase in yolk-sac development. The chorion is more immature, no mesoblastic tissue having appeared. There are fewer chorionic villi, they are shorter, and branching is minimal. The lacunar spaces are smaller and are not blood filled. The cap of blood overlying the implantation area and representing a physiologic "leak" in the system of intervillous spaces is not present. The latter supposedly occurs about the fourteenth day of development and is responsible for the not unusual vaginal spotting seen at the time of the first missed menstrual period.

Summary and Conclusions

1. An implanted, apparently normal human ovum, discovered by routine endometrial curettage in a patient with carcinoma in situ of the cervix, is described.

2. By correlation of menstrual, coital, and histologic data, the approximate age of the ovum is given as 13 days' gestational age.

3. The ovum is classified as a Carnegie Group 6 (Streeter) and consists of a well-defined chorion and chorionic cavity, primitive unbranched chorionic villi without mesoblastic component, bilaminar germ disc without definition of axis, primitive amnion, and distinct yolk sac.

4. Study of the yolk sac tends to support the evidence of Hertig and Rock that this structure arises independently and not through dissolution of the exocelomic membrane.

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THE HYDRIODIDE OF DIETHYLAMINOETHYL ESTER OF PENICILLIN G, NEOPENIL

IV. Placental Transmission of Penicillin Following Single Injections of Neopenil and Procaine Penicillin

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PREVIOUS studies[1-4] have demonstrated the placental transfer of penicillin from the maternal to the cord blood, following its parenteral administration to the antepartum mother; hence, the rationale for the widespread use of penicillin therapeutically in syphilis and gonorrhea of pregnancy and prophylactically in patients with prolonged rupture of the membranes.[2] However, all penicillin preparations do not cross the blood-placental barrier in a consistent manner.[5] Hence, the desirability of obtaining data on the behavior of the newer penicillin preparations.

A new penicillin ester, Neopenil* (the diethylaminoethyl ester hydriodide of penicillin G, known generically as penethamate hydriodide), has been shown to produce higher concentrations of penicillin in certain body tissues or organs than do the commonly employed penicillin salts. The concept of penicillin derivatives having affinity for certain tissues or organs of the body is not new, but this is the first instance in which the phenomenon has been observed to a degree that is therapeutically significant. Animal[6] and human[6-10] experiments have shown that Neopenil has a far greater affinity for the lungs than have the other penicillin preparations. In addition, animal experiments[6, 11] indicate a high penicillin level in the brain following the administration of the antibiotic in this esterified form. Experiments in human beings[12] have demonstrated unusually high penicillin levels in the cerebrospinal fluid following its administration. Since these unusually high tissue concentrations occur in the absence of high blood levels, it is felt that the tissue levels are due to the pharmacological property of the drug and not merely to a high blood-tissue diffusion gradient.[13] During the past year, this new penicillin compound has been studied at the Philadelphia General Hospital. It is the purpose of this paper to present data concerning the ability of Neopenil to cross the blood-placental barrier.

Methods

Upon admission to the labor room of the Obstetrical Department of the Philadelphia General Hospital, 186 pregnant women were assigned in rotation to one of two obstetrical services. The patients assigned to one service were given procaine penicillin, and those assigned to the other were given Neopenil. Both compounds were given as 500,000 unit intramuscular injections in aqueous suspension.

At the time of delivery, cord and maternal blood specimens were obtained. The sera from these were analyzed for penicillin by a *Sarcina lutea* cup-plate method.[14]

Results

The results are shown in Fig. 1 and Table I. The maternal blood levels of Neopenil and procaine penicillin were approximately the same up to the 4 hour period. However, the Neopenil cord levels were found to be statistically higher during this same period. In 96 per cent of the patients, either penicillin preparation was found to produce therapeutic cord levels of penicillin (0.03 U. per cubic centimeter or above) up to 24 hours after a single injection. There was no statistical difference between the cord levels produced by either type of penicillin during the 4 to 24 hour period. There was no toxicity noted from either penicillin.
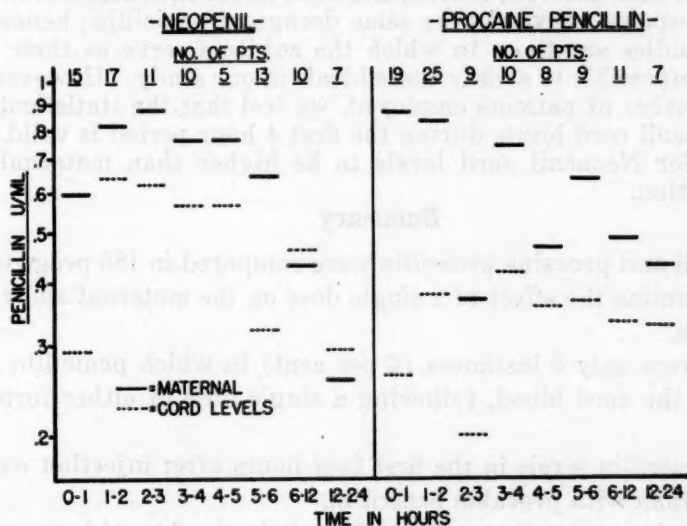
Fig. 1.

It should be noted that in the 6 to 24 hour interval, the penicillin cord levels in the Neopenil series become higher than the maternal levels. This may be an indication that Neopenil is excreted from the fetus at a slower rate than from the mother; however, inasmuch as this observation has been made on a minority of the series of patients, we mention it only as a subject for future investigation.

Comment

It would appear from this study that Neopenil furnishes somewhat higher penicillin levels to the fetus than does procaine penicillin. The therapeutic importance of this increased concentration is, of course, dependent upon the resistance of the infecting organism.

TABLE I.   PENICILLIN LEVELS FOLLOWING SINGLE INJECTION OF A 500,000 UNIT DOSE

HOURS AFTER INJECTION	NO. PATIENTS	MATERNAL		CORD		
		RANGE	AVERAGE	RANGE	AVERAGE	NO. < .03
Procaine Penicillin.—						
0-1	19	.16-2.65	.87	.03- .99	.26	0
1-2	25	.14-1.96	.84	< .03- .95	.38	1
2-3	9	.17- .55	.37	.12- .25	.19	0
3-4	10	.29-2.15	.75	.23-1.25	.42	0
4-5	8	.19- .89	.46	.13- .48	.36	0
5-6	9	.31-1.34	.64	.14- .92	.37	0
6-12	11	.22- .81	.49	.15- .79	.34	0
12-24	7	.045- .75	.43	< .03- .70	.33	1
Total	98					2
Neopenil.—						
0-1	15	.11-1.18	.59	.06- .57	.29	0
1-2	17	.10-2.09	.81	< .03-5.40	.64	2
2-3	11	.22-1.79	.87	.12-1.60	.62	0
3-4	10	.28-2.50	.75	.27-1.49	.56	0
4-5	5	.48- .94	.75	.30- .88	.56	0
5-6	13	< .03-1.58	.65	< .03- .81	.32	2
6-12	10	.04-1.04	.43	.18- .76	.46	0
12-24	7	.17- .34	.25	.09-1.01	.30	0
Total	88					4

It is known that different individuals even under identical conditions have varying dose-response curves to the same dosage of penicillin; hence, the best comparative studies are those in which the subjects serve as their own controls. It was impossible to satisfy these ideals in our study. However, because of the large number of patients employed, we feel that the statistical evidence of higher Neopenil cord levels during the first 4 hour period is valid, and that the tendency for Neopenil cord levels to be higher than maternal levels is worthy of mention.

Summary

1. Neopenil and procaine penicillin were compared in 186 pregnant women at term to determine the effect of a single dose on the maternal and cord-blood penicillin levels.

2. There were only 6 instances (4 per cent) in which penicillin could not be detected in the cord blood, following a single dose of either form of penicillin.

3. Cord penicillin levels in the first four hours after injection were higher with Neopenil than with procaine penicillin.

4. Cord levels greater than maternal levels in the 6 to 24 hour group seem to indicate that the penicillin level in the fetal blood is more prolonged after Neopenil than after procaine penicillin.

5. With the dosage employed, both preparations gave satisfactory cord levels over a 24 hour period.

6. No penicillin reactions were encountered.

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THE SIGNIFICANCE OF POLIOMYELITIS DURING PREGNANCY

An Analysis of the Literature and Presentation of Twenty-four New Cases

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DURING recent years, acute anterior poliomyelitis complicated by pregnancy has assumed an increasing prominence in the medical literature. Despite the numerous publications and the many cases reported (now near 600) the significance of this disease during pregnancy is not clear. In most previous studies, conclusions have been based upon the findings in small groups of patients, without attempt to correlate this information with data in the literature. Since there is much variance among these conclusions, it seemed desirable to make a collective analysis of all the cases which have been reported. In addition, we wish to present the details of 24 new cases which were observed at the Evanston Hospital.

Data

It has been possible to verify 586 cases of acute anterior poliomyelitis occurring during pregnancy which have been reported to date. In only 404 of these [1, 17, 20] were sufficient data presented to allow correlation, and in certain of these incomplete data made it necessary to exclude them from certain groups.

The 24 new cases which are presented represent approximately 3.7 per cent of 657 patients of all ages who were admitted to the Evanston Hospital with acute anterior poliomyelitis between the years 1945 and 1951. These cases are equivalent to 15.7 per cent of approximately 4,169 cases of acute anterior poliomyelitis which were treated in Cook County during this period.

Incidence

Table I shows the yearly incidence of poliomyelitis at the Evanston Hospital, including mortality figures, pregnancies, and sex distribution between the ages of 15 and 47 years.

It is frequently stated that pregnant women are more susceptible to the poliomyelitis virus than nonpregnant. There are no authentic data to support this claim. In our own experience, of 140 women between the ages of 15 and 47 with acute poliomyelitis, 17.1 per cent (24) were pregnant when the disease was contracted. There is no information as to what percentage of women of childbearing age are pregnant at any one time. Unless this is less than 17.1 per cent, there is no evidence that the pregnant woman is more susceptible than the nonpregnant. It is of incidental interest that in the preadolescents in this series, the disease is more common in boys. In the postadolescents, however, the frequency reversed itself and was almost twice as common in females.

The incidence by trimester is shown in Table II. It is apparent that the susceptibility to poliomyelitis does not vary with the stage of pregnancy. The

low incidence in the puerperium is about as one would expect for this relatively short period, since most of the cases occurred within two weeks of delivery.

TABLE I. POLIOMYELITIS AT THE EVANSTON HOSPITAL

YEAR	TOTAL NO. CASES	MORTALITY	PREGNANCIES	PATIENTS AGED 15 TO 47 YEARS	
				MALE	FEMALE
1945	41	5 (12.2%)	2 (4.9%)	5	7
1946	143	10 (7.0%)	4 (2.8%)	16	25
1947	60	0	1 (1.7%)	6	10
1948	67	0	0	3	20
1949	122	6 (4.9%)	7 (5.7%)	20	29
1950	71	6 (8.5%)	3 (4.2%)	15	16
1951	153	14 (9.1%)	7 (4.6%)	21	33
Total	657	41 (6.25%)	24 (3.7%)	86	140

TABLE II. INCIDENCE BY TRIMESTER INCLUDING MATERNAL MORTALITY
COMPOSITE OF 428 CASES

	NO. CASES	MORTALITY
First trimester	141 (33.0%)	8 (5.7%)
Second trimester	154 (36.1%)	11 (7.2%)
Third trimester	118 (27.7%)	18 (15.1%)
Post partum	15 (3.5%)	5 (33.3%)

The incidence of poliomyelitis in pregnancy according to age is shown in Table III. The highest incidence occurs in the age group 20 to 29 years, 67 per cent from our own series and 69.5 per cent in the review material corresponding to this age. Since the highest number of pregnancies also occurred in this age group, these findings are not surprising.

TABLE III. INCIDENCE AND AGE

AGE (YEARS)	342 CASES	EVANSTON HOSPITAL		
		PREGNANT	MALE	FEMALE (ALL)
15-19	49 (14.4%)	1 (4.2%)	31	40 (27.5%)
20-24	128 (37.5%)	6 (25.0%)	10	29 (20.6%)
25-29	109 (31.9%)	10 (41.6%)	21	35 (25.0%)
30-34	43 (12.6%)	5 (20.8%)	13	18 (12.8%)
35-39	13 (3.8%)	2 (8.3%)	6	11 (7.9%)
40	0	0	5	7 (5.0%)
Total	342	24	86	140

The incidence by parity is shown in Table IV. The parity was recorded in only 84 cases reviewed in the literature. Of these, approximately 75 per cent occurred in first and second pregnancies. A comparable incidence was found at the Evanston Hospital. The relatively low incidence in primigravid patients, and the high incidence in secundigravidas of our own series is considered to be happenstance rather than a reflection of predilection for second pregnancies.

TABLE IV. INCIDENCE AND PARITY

	84 CASES REVIEWED	EVANSTON HOSPITAL
Gravida i	26 (31.3%)	2 (8.3%)
Gravida ii	35 (42.2%)	13 (54.0%)
Gravida iii	14 (16.9%)	6 (25.0%)
Gravida iv	6 (7.2%)	1 (4.2%)
Gravida v	1 (1.2%)	0
Gravida vi	2 (2.4%)	1 (4.2%)
Unknown	0	1 (4.2%)

Mortality

The mortality rate in acute anterior poliomyelitis is extremely variable, and usually reflects the incidence of bulbar involvement in any given epidemic. Our own figures for over-all mortality (Table I) vary from 0 per cent to 12.2 per cent in the different years, the average being approximately 6.25 per cent. Among the 428 cases complicating pregnancy, the mortality rate was 9.7 per cent, a figure which is statistically higher than the death rate in the nonpregnant. With due regard to the possible difference in incidence of bulbar involvement and severity of the epidemic, this figure nevertheless suggests that the mortality rate is higher during pregnancy.

The maternal mortality by trimester (Table II) is of particular interest. Of 42 poliomyelitis deaths associated with pregnancy, more than one-half occurred during the last trimester and in the immediate puerperium. The period immediately following delivery appears to be the most critical time, since 12 per cent of the maternal deaths occurred in this small group which comprised only 3.5 per cent of the total cases of poliomyelitis associated with pregnancy.

The details of the two deaths which occurred at the Evanston Hospital are as follows:

The first patient was admitted in active labor with a fulminating bulbospinal infection. She was 25 years of age, gravida ii, para i, in the thirty-second week of gestation, and died undelivered shortly after admission. The other patient was the only pregnant patient with a "pure" bulbar infection. She was 23 years of age, gravida ii, para i. She was admitted to the hospital in the thirty-fifth week of pregnancy, critically ill with poliomyelitis, and bleeding violently from a central placenta previa. Delivery was accomplished by cesarean section under local infiltration anesthesia. The baby was stillborn, and the mother died of poliomyelitis on the fourth postoperative day. It was not determined in either case whether the baby had acquired poliomyelitis in utero.

Residual Paralysis

Of 147 cases from the literature in which residual paralysis is mentioned, there were 68 (46 per cent) patients who were paralytic to some degree. The degree of disability was impossible to estimate because of incomplete information. In the Evanston Hospital series, 15 (62.5 per cent) women had some degree of residual paralysis, while in 8 (33.3 per cent) the paralysis was considered to be disabling. As shown in Table V, among 116 women of childbearing age from our series who were not pregnant at the time of the poliomyelitis, 50 per cent showed a residual paralysis. This figure is shown to be statistically similar to the 63 per cent residual paralysis observed in the pregnant group. We therefore conclude that although the possibility of death from poliomyelitis is higher if the disease is contracted during pregnancy, nevertheless, if the patient survives, her chance of residual paralysis is no greater than if she were not pregnant.

TABLE V. RESIDUAL PARALYSIS

YEAR	ALL FEMALES, 15-47 YEARS	NONPREGNANT	RESIDUAL PARALYSIS	PREGNANT	RESIDUAL PARALYSIS
1945	7	5	4 (80%)	2	1 (50%)
1946	25	21	4 (19%)	4	3 (75%)
1947	10	9	5 (56%)	1	0 (0%)
1948	20	20	8 (40%)	0	0 (0%)
1949	29	22	13 (59%)	7	5 (71%)
1950	16	13	9 (69%)	3	2 (67%)
1951	33	26	15 (58%)	7	4 (57%)
Total	140	116	58	24	15 (63%)

Obstetrical Considerations

It is generally accepted that, irrespective of the stage of the disease or the extent of disability, poliomyelitis appears to have little if any effect upon uterine activity or development, nor does it impose any undue obstetrical hazard. The first and second stages of labor in our experience have progressed normally, and obstetrical complications of the third stage and immediate puerperium are similar in degree and incidence to those which are ordinarily expected. It is emphasized, however, that the presence of the abdominal tumor of pregnancy during the last three months may impose a considerable burden upon the patient's respiratory apparatus, which may be already embarrassed by excessive tracheobronchial secretions or by bulbar involvement. For these reasons particularly, a more liberal and prompt use of tracheotomy is urgently advocated. Horn[18] has emphasized that cesarean section at this time may be a lifesaving procedure. This is true especially after 32 weeks' gestation. In such cases it is suggested that cesarean section be performed irrespective of prematurity when respiratory embarrassment is not relieved by suction and tracheotomy.

Local anesthesia is preferred for any necessary procedure whenever it is easily feasible or when there is any respiratory embarrassment. Caudal and spinal anesthesia are interdicted in any patient who has or has had poliomyelitis. In the case which is uncomplicated by respiratory embarrassment, labor and delivery may be conducted along entirely orthodox lines. The judicious use of a cyclopropane-oxygen mixture in minimal amounts for these cases has proved satisfactory.

Fetal Considerations

Until recently, the fetus was thought to be well protected from maternal poliomyelitis by the placental barrier. At least two reports[19, 20] have now shown that placental transmission is possible, and further studies may reveal this occurrence to be more common. Poliomyelitis acquired in the neonatal period is always the result of maternal contagion, so that isolation methods must be established with this fact in mind. Rooming-in, therefore, is not a satisfactory method of isolating such patients.

There was pregnancy wastage in one-third of our cases at the Evanston Hospital. There were 5 abortions (20.8 per cent), all in the first trimester, 2 stillbirths (8.3 per cent), and 1 neonatal death (4.2 per cent). The neonatal death occurred in a 1,280 gram infant delivered prematurely at 37 weeks' gestation. It was not determined whether this child had acquired poliomyelitis. Although the incidence of miscarriage in this group is near the expected rate in patients who do not have poliomyelitis, and although the stillbirth and neonatal death rates are extremely high, nevertheless, this small series does not allow a conclusion as to whether these figures are significant.

A striking finding in the babies delivered at or near term was a birth weight which was distinctly subnormal for the period of gestation. This factor was prominent only in those patients who had acquired the disease in the first or second trimester of pregnancy. The infants were normal in all respects except that their general development and birth weight were significantly retarded. Three examples of this phenomenon occurred in secundigravidas who had previously been delivered of normally developed infants. After acquiring poliomyelitis during pregnancy, these patients delivered (1) a 1,280 gram infant at 37 weeks, (2) a 2,300 gram infant at 38 weeks, and (3) a 2,470 gram infant at 40 weeks, respectively. No explanation is offered for this occurrence.

Summary and Conclusions

A review of the literature dealing with acute anterior poliomyelitis in pregnancy has been made with the purpose of clarifying the implications of this combination of conditions. Of 586 cases reported, only 404 present sufficient detail to allow correlation. The details of 24 new cases, observed at the Evanston Hospital in the seven-year period, 1945 to 1951, are also reported.

The distribution of poliomyelitis according to trimester of pregnancy is even, showing no significant differences. Approximately two-thirds of the cases fall into the age group 20 to 29 years. Three-fourths of the cases occur in first and second pregnancies.

Among the 428 cases of poliomyelitis complicating pregnancy, the polio death rate was 9.7 per cent, a figure which is statistically higher than the polio death rate in the nonpregnant group. With due regard to possible differences in the incidence of bulbar involvement and the severity of the epidemic, this figure nevertheless suggests that the mortality rate is higher during pregnancy.

Although poliomyelitis appears to have no predilection for any particular trimester, it is significant that more than one-half of the maternal deaths occurred in the last trimester and in the immediate puerperium. The period immediately following delivery appears to be the most critical time, since 12 per cent of the maternal deaths occurred in this small group which comprised only 3.5 per cent of the total number of cases of poliomyelitis associated with pregnancy.

The occurrence of residual paralysis appears not to be influenced by pregnancy, the incidence being of the order of 50 per cent in both pregnant and nonpregnant groups. Thus, although the possibility of death from poliomyelitis is apparently higher if the disease is contracted during pregnancy, nevertheless, if the patient survives, her chance of residual paralysis appears to be no greater than if she were not pregnant.

Poliomyelitis appears to have little if any effect upon uterine activity or development, nor does it impose any undue obstetrical hazard. Pregnancy, labor, and delivery, in the absence of respiratory embarrassment, are conducted along entirely orthodox obstetrical lines. In the presence of respiratory embarrassment due to excessive tracheobronchial secretions, or bulbar involvement, the liberal and prompt use of tracheotomy is urgently advocated. After the thirty-second week of pregnancy, cesarean section may be a lifesaving procedure, since the presence of the abdominal tumor of pregnancy may impose a serious burden upon the patient's respiratory apparatus.

Pregnancy wastage occurred in one-third of the cases at the Evanston Hospital, and included 5 early spontaneous abortions, 2 stillbirths, and 1 neonatal death. Although no fetal defects occurred, data are presented which suggest that when poliomyelitis is acquired during the first or second trimester of pregnancy, babies delivered at term may show a significant retardation in general development and birth weight.

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THE EVALUATION OF THE WILLETT CLAMP SCALP TRACTION BY MEANS OF THE TOKODYNAMOMETER AND COMMENTS ON THE USE OF THE CLAMP*

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IT HAS been our clinical impression that scalp-clamp traction speeds labor in uterine inertia and is an efficient method of inducing labor. After Reynolds'[1] experiments with the tokodynamometer a method of recording uterine contractions was provided and it seemed logical to determine the effects of scalp-clamp traction on the frequency, amplitude, duration, and pattern of uterine contractions in normal labor, induction of labor, and uterine inertia.

Method and Results

The tokodynamometer is so constructed that a graphic representation of the exact amplitude, duration, and frequency of uterine contractions is accurately recorded. In each case, a lead of the tokodynamometer was placed on the abdomen over the fundus of the uterus and a second lead was placed over the area between the low and mid-zone of the uterus so that a continuous recording of the uterine contractions at the fundus and near the mid-zone was made.

Normal Labor

Group I consisted of nine patients in whom labor was normal. In each case the recordings of the uterine contractions were started while labor was still in the early phase and continued throughout labor. Approximately a half hour after the recordings were started the membranes were artificially ruptured and the clamp applied to the fetal scalp.

The application of the clamp is not difficult provided the cervix is at least 2 cm. dilated but if the cervix is undilated and uneffaced, the scalp clamp cannot be applied. With the fingers of the left hand used as a guide, the clamp is inserted through the cervix and the fetal scalp overlying the occiput is firmly grasped by the clamp. If the head is floating and the membranes are unruptured, an assistant firmly pushes the head into the pelvis before the membranes are ruptured and the clamp is applied.

Approximately thirty minutes after the application of the clamp the head of the fetus was pulled against the lower uterine segment by means of a half-pound weight which was attached to the scalp clamp by a cord. The weight was suspended by running the cord over a pulley. Thereafter, the weight was either removed or replaced at half-hour intervals until delivery. The tracings of the uterine contractions at the fundus and miduterine zone recorded during the period of scalp-clamp traction were compared with recordings made while

no traction was being exerted. A careful comparison was made in regard to amplitude, frequency, and duration of contractions. The recordings were also examined for any evidence of change to or from fundal dominance of contraction.

Scalp traction made no change in amplitude, frequency, or duration of uterine contractions (Fig. 1, *A* and *B*). In every case, the contractions of the fundus were of greater amplitude than those of the midsegment.

Uterine Inertia

Group II was composed of two patients who had uterine inertia and in both cases the pelvis was proved to be normal by x-ray pelvimetry. The leads of the tokodynamometer were placed as previously described. Labor had been established for an average of 12 hours before recordings of the uterine contractions were started. In each case, after recording the uterine contractions for about a half hour, the scalp clamp was applied to the fetal head but no traction exerted. Thirty minutes later a half-pound scalp traction force was applied and alternately removed and applied as described in the cases in Group I. A continuous recording of the uterine contractions was made for 7 hours in each case. The recordings were examined as in the cases in Group I.

Scalp-clamp traction made no change in amplitude, frequency, or duration of contractions in two patients with uterine inertia nor did traction by the scalp clamp produce any shift of uterine activity from the midsegment to the fundus (Fig. 1, *C*).
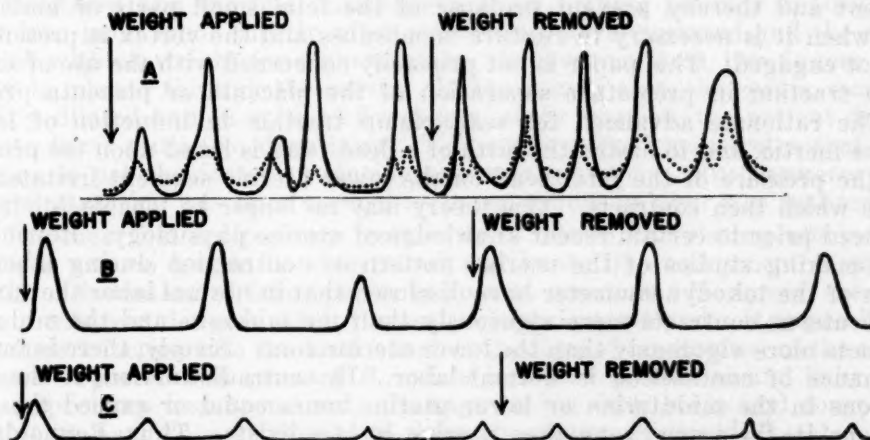
Fig. 1.—*A*, The solid line represents fundal activity and the dotted line represents the activity at the lower portion of the uterus. Scalp traction (weight applied) has not increased the duration, frequency, rate, or amplitude of contractions.

B, Tracing representing fundal activity taken in early labor showing no increase in amplitude, duration, rate, or frequency of uterine contractions with scalp traction (weight applied).

C, Tracing representing the fundal activity in uterine inertia. Scalp traction (weight applied) has not improved the rate, amplitude, frequency, and duration of contractions.

Induction of Labor

In Group III were four patients in whom an elective induction of labor was attempted by means of scalp-clamp traction. The leads from the tokodynamometer were arranged as previously described. In each case, after recordings of the uterine activity were noted for one-half to two hours, membranes were ruptured and the scalp clamp applied without weight for traction.

After thirty minutes in the first two, and two hours in the second two cases, the half-pound weight was applied. Thereafter, the scalp traction was alternately applied and removed as described in cases in Group I save that in two cases the interval between the change of weight was two hours or over. In every case recordings were made for three hours or longer after the scalp clamp traction had been applied. In two cases within five minutes after the rupture of membranes and application of the clamp without traction the uterus was contracting every eight minutes. Contractions were lasting one and one-fifth minutes in one case and one and one-half minutes in the other. The contractions were of good amplitude. In the third case also labor started before the weight was applied to the scalp clamp. In the fourth case the cervix was only slightly dilated and it was only with the greatest difficulty that the clamp was applied to the fetal scalp. In spite of the weight being applied to the clamp for five hours, the patient did not go into labor until forty-one hours later. Scalp-clamp traction made no change in amplitude, frequency, or duration of contractions and did not initiate labor (Fig. 1, B).

The scalp clamp caused no maternal or fetal damage of significance in any of the cases presented in this paper.

Comment

Scalp-clamp traction has been advocated in uterine inertia, induction of labor, to hasten the birth of a dead fetus, malpresentation of the vertex, premature separation of the placenta, and placenta previa. It has also been employed to bring the floating fetal head into apposition with the lower uterine segment and thereby prevent prolapse of the fetal small parts or umbilical cord when it is necessary to rupture membranes and the vertex is presenting but not engaged. This paper is not primarily concerned with the use of scalp-clamp traction in premature separation of the placenta or placenta previa.

The rationale advanced for scalp-clamp traction in induction of labor, uterine inertia, and to hasten the birth of a dead fetus is based upon the premise that the pressure of the fetal head on the lower uterine segment irritates the uterus which then contracts. This theory may no longer be tenable for it was advanced prior to certain recent knowledge of uterine physiology. Reynolds'[1] epoch-making studies of the uterine pattern of contraction during labor by means of the tokodynamometer have disclosed that in normal labor the fundus of the uterus contracts more vigorously than the mid-zone and the mid-zone contracts more vigorously than the lower uterine zone. Simply, there is fundal dominance of contraction in normal labor. In contradistinction, if the contractions in the miduterine or lower uterine zones equal or exceed the contractions in the upper zone then uterine inertia exists. Thus, Reynolds indubitably demonstrated that it is not only the contractions of the uterus that produce expulsion of the fetus but it is the pattern of the uterine contractions that is of paramount importance. In view of these revelations it does not seem credible that simple pressure of the fetal head against the lower uterine segment could reverse the abnormal activity of the mid-zone and lower zones and promote fundal dominance of contraction.

One of us[2] compared the length of labor in cases in which the clamp was used to the length of labor in cases in which the clamp was not used and concluded that the scalp clamp speeded labor. This work was done before the frequent use of x-ray pelvimetry and therefore no attempt was made to measure the pelvis by x-ray. From this comparison it is possibly erroneous to deduce that the uterus contracts more efficiently after scalp traction is applied. Before this conclusion can logically be entertained it will be necessary to know and compare the size of the pelvis, the size and malleability of the fetal head,

and rigidity of the cervix. One of us[3] has shown that mensuration of the maternal pelvis without x-ray is usually inaccurate and it is stated that unless x-ray pelvimetry is resorted to, even the diagonal conjugate cannot be evaluated accurately.

Eastman[4] believes that the premature and injudicious use of large amounts of analgesic drugs is the most common cause of uterine inertia. Exactly what part is played by sedation in uterine inertia is not known. Earlier reports[2, 5] on the use of the scalp-clamp traction in uterine inertia do not consider the kind and amount of sedation or the stage of labor at which the sedation was administered. Unless these factors are considered this might negate the reliability of comparing the length of labor in various cases.

If the fetus is in the vertex presentation and the patient is standing erect, more than one-half pound pressure is exerted against the lower uterine segment by the weight of the fetus and amniotic fluid and this does not initiate labor. (The force exerted by scalp traction is usually under one-half pound.) In an earlier report two of us[5] stated, "The average duration of the latent period between the application of the clamp and the onset of labor in 38 cases was one hour and 24 minutes." The crux of this situation can readily be explained when it is noted that the cervix must be several centimeters dilated and the membranes must be ruptured before the scalp clamp can be applied. This is precisely the type of case that goes into labor whether a scalp clamp is applied or not. Certainly, the length of time necessary for the induction of labor in these patients cannot be equally compared with the length of time necessary for induction of labor in patients in whom the cervix is undilated and uneffaced and the fetal membranes intact. Three patients in Group III went into good labor shortly after membranes were ruptured and the clamp applied without weight for scalp traction. In these patients, two fingers could easily be placed through the cervix. In the fourth case, the cervix was only slightly dilated and in spite of five hours' scalp traction, the patient did not go into labor until two days later. This apparently demonstrates that scalp traction is not the factor producing the onset of labor. Furthermore, when the scalp traction was later applied no improvement in labor was realized.

The idea that scalp-clamp traction is of use in stimulating uterine contractions can no longer be entertained and hence its employment in uterine inertia or induction of labor per se is open to question. Moreover, there are certain inherent dangers when the scalp clamp is employed. It is possible to introduce infection into the birth canal at the time of application of the clamp. Browne[6] reported two cases of B. welchi infection of mother and baby after the scalp clamp had been used. Damage to the fetal brain and consequent fetal death have been attributed to the scalp clamp. Kaltreider[5] states, "The complications to the fetal scalp were as follows: cellulitis, . . . abscess of the scalp, . . . hematoma, . . . and laceration. . . ." Since his article was written it has become routine at the University of Maryland Hospital to give an antibiotic to the prospective mother as soon as the clamp is applied. The baby is given an antibiotic after delivery. Since the initiation of this routine, other than local necrosis of the fetal scalp or hematoma, there has been no complication to mother or infant due to the scalp clamp.

In contradistinction to condemnation of employment of scalp traction for the purpose of stimulating or initiating uterine contraction, scalp traction still may be considered part of the armamentarium of the most modern obstetrician, for it is useful in certain cases of marginal placenta previa. The scalp traction can be used to bring the fetal head into juxtaposition against the bleeding portion of the separated placenta and thereby aid in controlling bleeding. After malpresentation of a fetus has been manually corrected, the

scalp clamp may be employed to maintain the vertex presentation until engagement occurs. However, the foremost indication for the use of scalp traction is in the occasional case in which it is necessary to rupture membranes to initiate labor even though the fetal head is floating.

Conclusion

Scalp-clamp traction in this series was ineffective in stimulating uterine activity in normal labor, uterine inertia, or in the induction of labor.

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STUDIES ON RESUSCITATION. AN EXPERIMENTAL EVALUATION OF THE BLOXSOM AIR LOCK*

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THE Bloxsom[1] air lock is a relatively new device for infant resuscitation. The principle upon which its construction was based was Bloxsom's[2] original idea described in 1942: "a hidden purpose [of labor] is found in the prelabor contractions and resulting pressures leading to respiratory effort."[2] In a series of 100 deliveries by cesarean section, he[3] found that much more "difficulty in respiration" was present in those infants not subjected to a trial of active labor, and hypothecated that "the lack of conditioning of the respiratory center . . . by uterine contraction" was one factor in the high incidence of difficulty in beginning respiration.

In an effort to simulate the changing pressures of uterine contractions, a chamber was constructed into which a pressure control was built allowing for the application of alternating and variable pressures to the chamber at different rates. The suggested pressures are approximately those of uterine contractions, ranging from one to three pounds (50 to 150 mm. Hg). The suggested duration of each cycle is from 40 to 45 seconds, producing about 1.2 cycles per minute. Other advantages of the air lock are stated to be better removal of fluid from the infant's lungs by "expansion of gases," better absorption of oxygen through the skin, prevention of pulmonary edema and more efficient aeration of atelectatic lungs.[2]

Although Bloxsom has not recommended the use of the air lock specifically for apneic infants, his use of the terms "asphyxiated newborn infant" and "resuscitation" implies that apnea may well be present in some cases. He is at present assembling data of oxygen saturation measured with a photoelectric cell on the ear of the infant before and after "processing" in the air lock.[4] We look forward with interest to the results of this study.

Since the published results of this type of resuscitation have been based wholly upon clinical impressions, it seemed wise to investigate the efficiency of the device under controlled experimental conditions.

Methods

Healthy dogs (weighing 5 to 10 kilograms) were injected intravenously with pentobarbital until anesthesia was produced. A femoral arterial cannula and a cuffed endotracheal tube were then inserted. A relaxant, usually Syncurine, was administered intravenously until apnea was induced, and additional drug given as needed to insure the maintenance of apnea. The air

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lock was ventilated for several minutes with equal amounts of compressed
air and oxygen, at a total flow of 16 liters per minute prior to placing the dog
in the chamber.   The apneic animal was then placed in the lock and cycling
begun immediately.   The pressure in the lock reached 3 pounds in 38 seconds,
and fell to 1 pound in 7 seconds.   The animal was kept in the lock until the
heart beat was no longer visible, or until respirations reappeared with regu-
larity.   Blood samples were taken before and after "processing" in the lock
and after resuscitation by other means.   These were analyzed for oxygen and
carbon dioxide content by Van Slyke's method.[5]   pH determinations were
made with Holaday's[6] modification of the Cambridge glass electrode and
carbon dioxide tensions were calculated.   Gas analysis of the contents of the
chamber were made by Haldane's method.[5]   Some of the dogs were placed in
the lock in a severely hypoxic state, while others were ventilated with 100
per cent oxygen using a manual inflator for several minutes prior to intro-
duction.   After removal from the lock, the dogs which appeared dead or
markedly depressed were again ventilated manually.
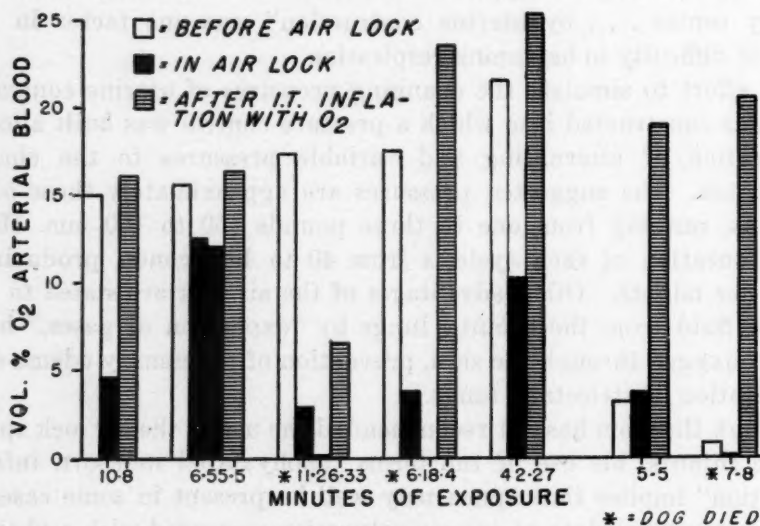
Fig. 1.—Oxygen values—apneic dogs in air lock.

In some experiments, barbiturates combined with relaxants were used
to depress but not to abolish respiration.   Arterial cannulation, endotracheal
intubation, and blood sampling were performed as stated above.

In order to study the movement of dye-stained fluid in the bronchus of a
dog during apnea and exposure to the air lock, methylene blue or a suspension
of India ink was introduced endobronchially and the animal sacrificed later.

Results

In 13 experiments on 9 dogs apnea was produced and the animal was
placed in the air lock.   In 9 experiments the animal remained apneic and was
removed in periods of from 2 to 18 minutes for resuscitation by inflation of the
lungs with oxygen.   Seven of these animals could not be revived.   In all
cases the oxygen arterial content fell from 25 to 100 per cent of the value ob-

tained before the animal was placed in the lock, with the exception of one case in which the oxygen content changed slightly from 3.1 to 3.7 volumes per cent in two minutes. This animal was removed from the chamber because of an invisible cardiac impulse. In these nine apneic dogs, the carbon dioxide content of arterial blood increased 2 to 70 per cent above the control measurement.

In 4 experiments, respiratory effort returned to some degree while the animal was still in the lock. Two of these four animals did not survive the experiment even though they were left in the lock from 30 to 60 minutes. The oxygen values in these animals also fell from 20 to 100 per cent and the rise in the carbon dioxide content was even higher than in the dogs which remained apneic.

In 3 experiments in apneic dogs frequent measurements of arterial blood pH, oxygen saturation, and tension of carbon dioxide were made. In all 3 cases there was a rapid fall in pH within a minute of entrance into the air lock, a rise in carbon dioxide tension from two to five times that of the control value, and a marked fall in oxygen saturation.

APNEIC DOGS
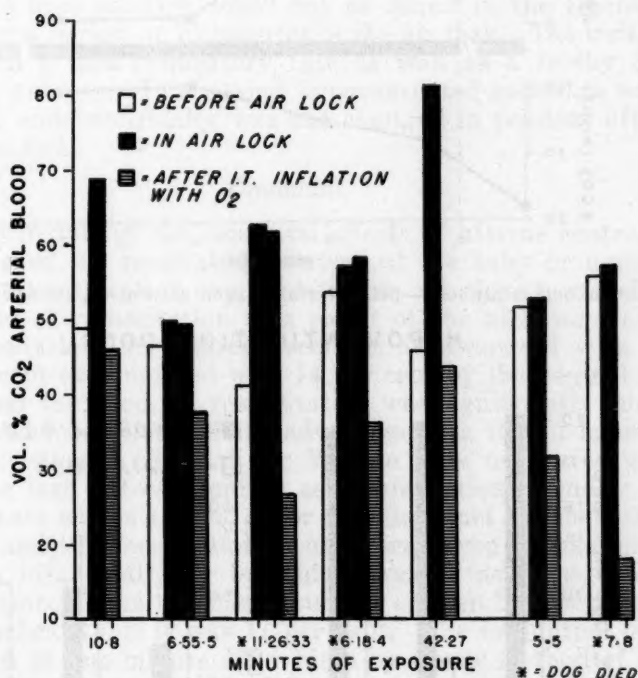
Fig. 2.—Carbon dioxide values—apneic dogs.

After removal from the air lock, the arterial oxygen and carbon dioxide contents were improved significantly in all the surviving animals by manually administered intermittent inflations with oxygen.

From these data it was concluded that, under these conditions, the use of the air lock was inadequate to resuscitate apneic dogs.

Hypoventilation Experiments

In 6 dogs, respiratory depression short of apnea was achieved principally by the use of an intravenous barbiturate, with the addition of a relaxant in 3

cases. After periods of 28 to 268 minutes blood gas studies showed that oxygenation was improved and carbon dioxide retention did not occur.

It was concluded that in the presence of established but depressed respiration, not preceded by a period of apnea, the air lock provided satisfactory ventilation of dogs, under the conditions of these experiments.
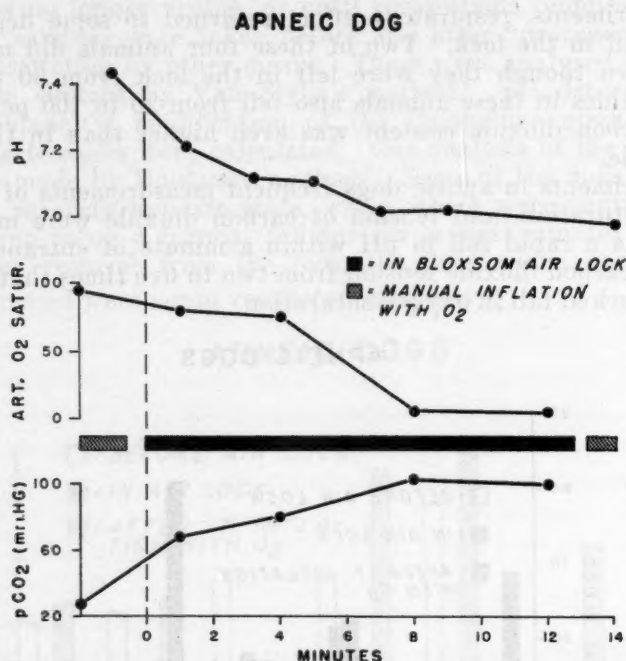
APNEIC DOG

Fig. 3.—Apneic dog in air lock—pH, arterial oxygen saturation, carbon dioxide tension.

HYPOVENTILATION-DOGS
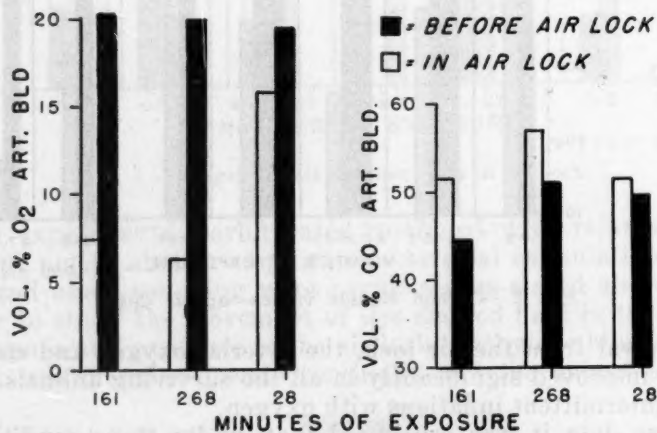
Fig. 4.—Oxygen and carbon dioxide values—hypoventilated dogs in air lock.

Removal of Carbon Dioxide From the Air Lock

Since the use of the lock has been recommended for several days for cyanotic infants, the problem of carbon dioxide removal from the chamber is

of more importance than with the usual resuscitator. Although the carbon dioxide production of the dog and the type of skin differ greatly from those of a newborn infant, it was thought that the problem of simple removal of carbon dioxide could be studied satisfactorily. In two of the hypoventilation experiments, a sampling catheter was placed near the nose of the dog and samples withdrawn at intervals. At a flow of 16 L. per minute, with a cycling rate of 1.2 times per minute, the carbon dioxide content of the air in the chamber was 0.44 per cent after 40 minutes in one experiment, and in the other it rose from 0.03 per cent in six minutes to 1.46 per cent in 120 minutes. It seems probable that unless the lock is opened frequently for purposes of nursing care, there is danger of excessive accumulation of carbon dioxide.

Removal of Secretions and Prevention of Pulmonary Edema

Bloxsom has reported that this device aids in removing secretions from the lungs by changing the size of a gas bubble at the periods of high and low positive pressure. At the lower level of positive pressure, the bubble is relatively larger and forces any secretion proximal to it up toward the trachea. In one dog in moderate respiratory depression, endobronchially placed methylene blue solution could not be found in the trachea or upper air passages after a period of 70 minutes in the air lock. The irritation of the solution produced a fast respiratory rate as well as a frothy fluid in the bronchus seen at autopsy. In a second hypoventilated animal, a suspension of India ink placed endobronchially was not changed in position after a period of one hour in the lock.

Comment

The whole principle of the beneficial effects of uterine contractions upon the "conditioning of the respiratory center" of the baby or upon any other mechanism of fetal respiration or circulation is not clear to us. Bloxsom devised this method of resuscitation as a result of the high number of infants "requiring resuscitation" in cesarean sections as compared with normal deliveries (42 per cent as compared with 14 per cent by the vaginal route). He further states that the need for resuscitation was significantly more frequent in those infants who had not had the advantage of a test of labor. Our own experience at the Sloane Hospital for Women does not agree with that of Bloxsom. In the last 122 consecutive cesarean sections, equally divided between those patients with a trial of labor and those not in labor, the incidence of the need for assisting respiration in any form, even insufflation of oxygen over the face in infants already breathing, was 27 per cent, while in those infants needing more active treatment, such as oxygen by positive pressure by mask or endotracheal tube, it was 17 per cent. The evaluation of the condition of the infant at one minute after birth by a new method of coding, and with trained observers, revealed no difference between those infants who had been subjected to active uterine contraction and those who had not.

Ahlfeld,[7] whose paper in 1905 is quoted in support of Bloxsom's theory, specifically states that uterine muscular contractions had no effect upon the many tracings of fetal intrauterine respiration he recorded.

Efficiency of Ventilation

The principles of adequate ventilation during apneic states have been well discussed by Barach.[8] Thunberg's work in 1926[9] with the barospirator marks the first advance in this field, but it was soon found that apnea could not be prolonged for more than a few minutes, unless the subject took one or

two breaths from time to time. By construction of an alternating pressure
chamber Barach was able to demonstrate other factors necessary for main-
taining apnea. One of these factors is the necessity of equalizing the pressures
entering the mouth with that applied to the chest wall. The pressure neces-
sary to overcome the resistance of the tracheobronchial tree was found to be
between 5 and 6 cm. water in the average-sized adult. If the application of
pressure to the chest wall is slightly delayed until that in the trachea is 5 cm.,
an apneic state can be maintained for hours. This delay can be brought about
by a machine constructed with a separate head piece, or by the introduction of
a baffle plate between the head and shoulders. No such device for equalizing
pressures is present in the Bloxsom air lock. Barach also confirmed Thun-
berg's original recommendations for the amount of alternating pressures (2
pounds) and for rate of application of these pressures. The air lock provides
a variation of 2 pounds pressure, but the rate of cycling as described is much
too slow to provide ventilation in an apneic patient. An alternation of pres-
sures at a minimum of 25 times per minute was necessary in both Thunberg's
and Barach's patients, while that advised in the air lock is in the range of 1.2
times per minute.

It is interesting to calculate the amount of gas which can be delivered to
the lungs by compression of gas mixture in the chamber. At alterations of 1
to 3 pounds pressure, and at a rate of 1.2 cycles per minute,[10] 12 c.c. of gas
can be made to enter the lungs. Since the pulmonary ventilation in the infant
during the first day averages 835 c.c. per minute[11] while during the first hour
it is more likely nearer 500 c.c. per minute[12] only a very small fraction of gas
needed for ventilation can be supplied by molecular compression.

Promotion of Bronchial Drainage

This use of the air lock is described by Bloxsom as being one of its most
important indications. Barach[13] has recently reviewed the principles of sud-
den decompression of pressure to produce an expulsive cough. Both in ex-
perimental work and practically in patients with pulmonary disease, removal
of bronchial secretions can be effected by sudden decompression with 2
pounds pressure, during a very brief interval, 0.06 second. Expansion of
gases behind the secretions, and their sudden decompression pushes secretions
to larger bronchial divisions. This decompression can be obtained by sudden
application of positive pressure to the chest, then decompression to atmospheric
pressure. This theory obviously takes for granted that some air is already in
the lungs in order to be decompressed, a situation frequently not present in the
apneic newborn infant. The Bloxsom apparatus has none of these mechanical
properties.

Absorption of Oxygen Through the Skin and Mucous Membranes

Bloxsom has stressed the fact that, since the newborn infant, especially
the premature infant, in the air lock is exposed to 1 to 3 pounds of tension
over atmospheric pressure, in an atmosphere of at least 58 per cent oxygen
some oxygen diffuses through the infant's thin skin, well supplied by blood.
It is further implied that such oxygen is available for general metabolism.
Since Gerlach's[14] studies in 1851, experimental workers have endeavored to
prove or disprove this point. The general method of study has been to
measure the amount of oxygen which disappears from a mixture of gases
tightly applied to the skin, or surrounding the lower half of the body. In
spite of technical difficulties and the questionable methods of gas analysis
used in the nineteenth century, in no case has it been shown that oxygen

which is removed from such mixtures is available for metabolism other than that of the skin itself. By calculations in the adult, it has been estimated that not more than 1 per cent of pulmonary respiration can be carried out by the total area of skin.[15] No work has been done to date on the skin of the premature infant, but Sametinger[16] attempted to improve the blood supply of the adult skin by inflammation with the application of mustard paste, or iodine solution. Through this inflamed area he found slightly increased absorption of oxygen.

Absorption of oxygen through the mucous membranes has been studied sporadically. Moore and Cochran[17] studied the absorption of oxygen through the colon and rectum in anoxic dogs, through a cecostomy, and found no significant improvement in the blood arterial oxygen content or saturation. Galdston and Horwitz[18] have recently studied the rate of exchange of oxygen and carbon dioxide in the supraglottic portion of the respiratory dead space during breath holding, and found slight disappearance of oxygen from the gases in the dead space. There was no evidence produced that this oxygen diffused further than the salivary secretions. No blood studies were made. Further studies in this field are necessary.

Clinical Impressions

In many obstetrical services, the clinical impression exists that the condition of the infant is improved by placing him in the air lock.[19] Indeed, the condition of any anoxic patient should be improved by placing him in an atmosphere of at least 50 per cent oxygen, under a tension of more than 50 mm. Hg above atmospheric pressures. There is no evidence that any improvement in the infants is related to the alternating pressures simulating uterine contractions.

Conclusions

1. In adult dogs in which hypoventilation was produced by drug depression, oxygenation and removal of carbon dioxide proceeded satisfactorily in the Bloxsom air lock, in an atmosphere of 58 per cent oxygen at pressures varying between 810 and 910 mm. Hg, at a cycle of 38 and 5 seconds.

2. In adult dogs made apneic by drug depression, the Bloxsom air lock was unsuccessful in all cases in oxygenating the animals and removing carbon dioxide.

3. An analysis was made of other suggested advantages of the air lock. They appear to be unsubstantiated in respect to removal of fluid from the lungs, and absorption of oxygen by the skin.

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BLOOD LOSS DURING GYNECOLOGICAL OPERATIONS*

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DURING the past decade our surgical horizon has been extended. We utilize radical surgery in the treatment of carcinoma and we operate on members of an older segment of the population who would have been dismissed previously as unsuitable surgical candidates. From all current indications it appears that these practices will continue. In fact, Kosmak,[1] Zeman and Davids,[2] and Lash[3] have discussed this trend of treating older age groups. However, as we extend indications for surgery we find that we must, more than ever before, maintain a state of equilibrium in the patient during the preoperative, postoperative, and operative periods.

There are many phases to this problem of controlling a surgical patient and frequently each phase is complicated further by associated medical conditions. However, through this entire problem very few conditions can be found which are as amenable to correction as operative blood loss. Before one is in a position to replace blood, though, he must have some idea of the quantity required. Unfortunately, the estimation of blood loss is notoriously inaccurate. Our experience showed that the differences between the estimated and the measured loss were often as much as 400 to 500 c.c. Not only will the surgeon underestimate the loss, but far too often marked disagreement will be evident between the surgeon, assistant, and anesthetist at the same operation. The youthful patient in good health may be able to tolerate these errors in estimation, but the elderly patient in poor health has a much narrower margin of safety, and estimation of blood loss is frequently inadequate for proper care. It is necessary then to find some other means of determining the deficit in blood volume.

The literature offers very little with regard to blood loss during gynecological operations, but it does disclose various methods of measuring the loss. The first satisfactory report was made in 1924; Gatch and Little[4] found about a 200 to 300 c.c. loss during standard abdominal hysterectomies. Then Pilcher and Sheard[5] in 1937 noted a 650 c.c. loss during a vaginal hysterectomy. In the years following reports were scattered,[6-14] and gynecological procedures were included among other surgical operations. The over-all recorded losses ranged roughly between 50 c.c. and 1,500 c.c. for abdominal hysterectomies, but the total number reported was only about 100 cases. Comparatively few vaginal procedures were investigated. From an analysis of the foregoing it was evident that far too many variants entered the picture, and that oftentimes cases were selected. Results from one clinic or hospital could not necessarily be applied

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to another. The amount of blood lost during gynecological operations had been estimated in the Lying-In Hospital, and in the realization that it was inaccurate, a program of more definite measurement was undertaken.

Two satisfactory methods for the measurement of operative blood loss were found to be in vogue, the so-called colorimetric and the gravimetric. In the case of the colorimetric,[4, 5, 12] the blood-stained sponges and drapes are washed in dilute hydrochloric acid or sodium bicarbonate, and the recovered dissolved hemoglobin is assayed with a photoelectric colorimeter. Then conversion to blood loss is easily carried out. The gravimetric technique[13-16] differs from the latter in that the quantity of blood lost is determined by weight. Fortunately, sponges and towels in a dry state are fairly uniform in weight, and since we are at liberty to assume that 1 c.c. of blood will weigh 1 Gm., the numerical difference between the weight of the soaked and dry sponge will equal the number of cubic centimeters of blood lost. Dry sponges are almost always used but, if for any reason dry sponges are considered hazardous for the patient or are not in accord with the surgical technique, well wrung out, moist sponges may be substituted. The weight of the well wrung out sponge or abdominal gauze is taken instead of the dry weight. In addition, it is possible to keep a running account of the blood loss during the course of the operation.
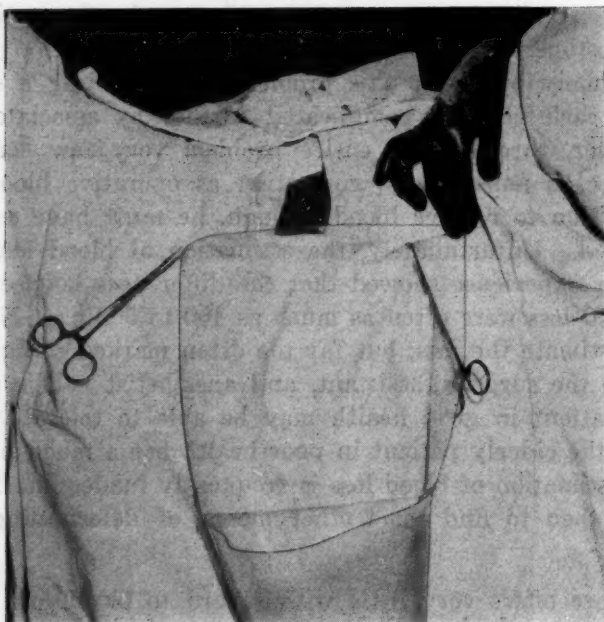
Fig. 1.

The gravimetric method was employed for our study. The only piece of equipment required is an ordinary dietitian's scale.[16] However, it was necessary to refine the technique of collecting blood during vaginal operations, for at times the loss on heavily soaked drapes was extremely difficult to assess. To overcome this obstacle a plastic bag was designed which can be sewn to the fourchette and clamped to the drapes. This bag will collect almost all of the free blood escaping from the operative site (Fig. 1).

Material

In the early part of 1951 a policy of measuring blood loss was instituted. Many different gynecological operations were studied but, for the purpose of

analysis, it soon became apparent that the investigation would have to be restricted to the standard procedures. These were abdominal total hysterectomies, anterior and posterior repairs, Manchester type plastics, vaginal hysterectomies, and radical hysterectomies with lymph node dissection (Wertheim operations). Consecutive cases could not be followed, but at no time were selections or deletions made, other than for the availability of personnel to measure the blood loss. Seventy-seven hysterectomies, 64 vaginal procedures, and 10 Wertheim operations were accumulated, and the age distribution of this group paralleled that of the total 1951 clinic population undergoing the same types of operations. Both private and pavilion cases were included, the majority being pavilion, and many members of the attending and resident staffs contributed to the series. Thus, a fairly representative sample was obtained.

Results

The average blood loss in 77 abdominal total hysterectomies was 678 c.c. This is somewhat above most reported figures. The minimum was 109 c.c. and the maximum was 2,000 c.c. In the latter case the patient's tissues were extremely friable; she was transfused preoperatively after being admitted for menorrhagia with an initial hematocrit of 19 per cent (Table I).

TABLE I.   BLOOD LOSS IN CUBIC CENTIMETERS IN 77 ABDOMINAL HYSTERECTOMIES

Maximum	2,000
Minimum	109
Average	678
Median	608

Hysterectomies were performed under Pentothal-nitrous oxide-oxygen-ether anesthesia with tubocurarine supplements. We did not employ hypotensive techniques. The abdomen was opened through a midline or transverse incision and the cervix was removed after a dissection of the paracervical fascia was carried out. In most cases the rate of blood loss began to mount after the uterine vessels were ligated and the dissection of the paracervical fascia was begun. Therefore, I would assume that blood loss during a total hysterectomy would be greater than during a subtotal hysterectomy but, since we perform relatively few subtotal hysterectomies, the figures in these groups cannot be compared statistically.

TABLE II.   BLOOD LOSS IN CUBIC CENTIMETERS IN VAGINAL PLASTIC OPERATIONS

OPERATION	NO.	MAXIMUM	MINIMUM	AVERAGE
Vaginal hysterectomy	16	1,374	260	716
Manchester	22	1,970	265	849
Anterior and posterior repair	26	1,640	160	556
Total vaginal	64	1,970	160	701

Sixty-four vaginal operations were studied. Sixteen were vaginal hysterectomies, 22 were Manchester procedures, and 26 were anterior and posterior repairs (Table II). The largest average blood loss was in the Manchester type; this was 849 c.c. with a maximum of 1,970 c.c. and a minimum of 265 c.c. Vaginal hysterectomies followed with an average of 716 c.c. and ranged between 260 c.c. and 1,374 c.c. Finally, anterior and posterior repairs averaged 556 c.c. The maximum in this group was 1,640 c.c. and the minimum 160 c.c. An anterior and posterior repair is performed in our clinic for the correction of a

cystocele and rectocele, whereas the Manchester procedure is employed for an
associated first or second degree descensus, or a third degree descensus in a
young patient, with a diseased cervix. Vaginal hysterectomy is reserved pri-
marily for second and third degree descensus or in cases where future child-
bearing is of no importance. In all of our vaginal procedures a thorough re-
pair anteriorly and posteriorly is done, which most likely explains why the
blood loss in the Manchester procedures and vaginal hysterectomies is greater
than the loss in the simple anterior and posterior repairs. The steady ooze
from the amputated cervix is probably the contributing cause for the greater
loss in the Manchester group.
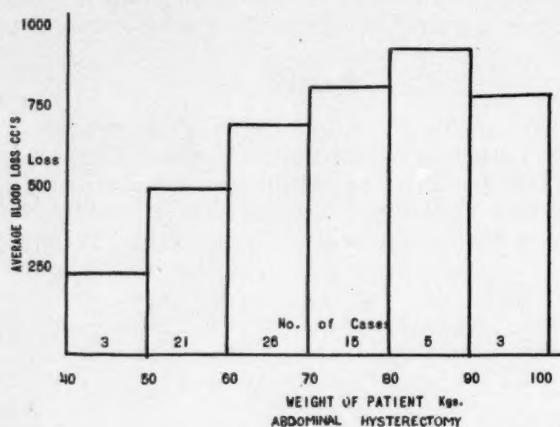
Fig. 2.
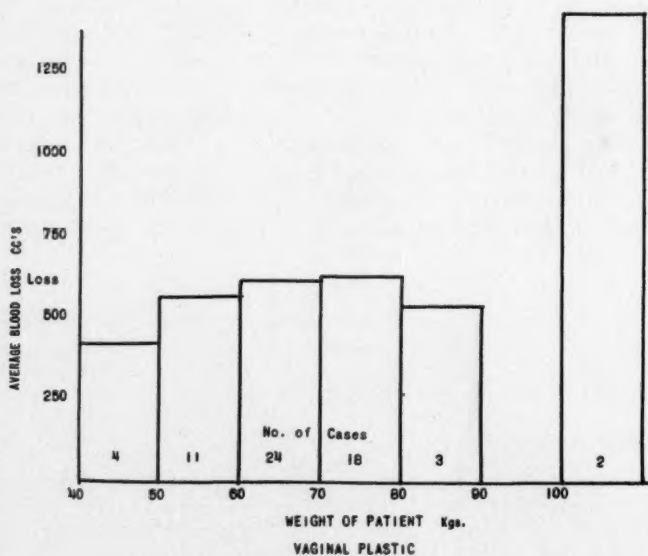
Fig. 3.

Needless to say, many operators were quite surprised to find that the
blood losses were as great as were determined. The excessive loss in some
cases stimulated further interest in the subject and attention was directed
toward factors and circumstances which may influence the amount. Obviously,
if we could learn what the factors are, we could anticipate and be prepared

for a blood loss in excess of average, and could keep abreast of a loss which may cause shock. The weight and age of the patient, the duration of the operation, and the nature of the pathology were investigated with this in mind.

As evident from Fig. 2 there appears to be a definite correlation between the weight of the patient and the blood lost during abdominal hysterectomy. The heavier the patient, the greater the blood loss. Poor exposure and less adequate hemostasis deep in the pelvis and parametrial regions may account for the increase in the obese patient. Excessive blood loss from the abdominal incision was not responsible for the discrepancy.
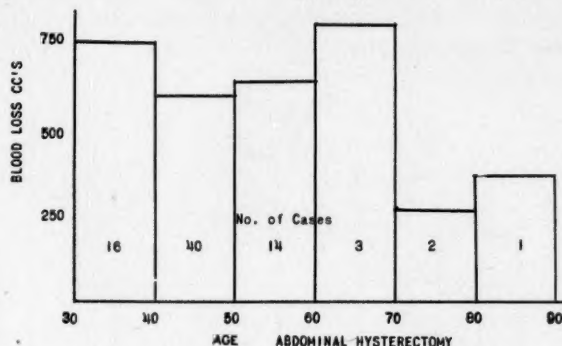
Fig. 4.
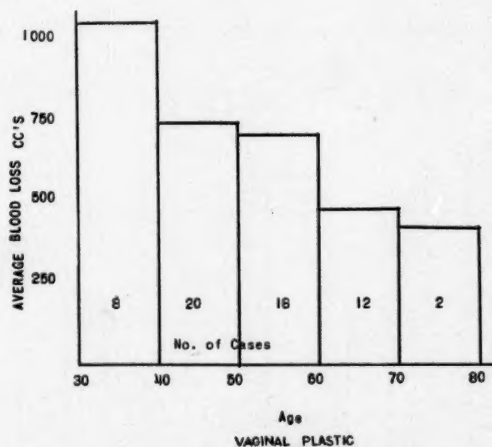
Fig. 5.

The same distinct relationship of blood loss to weight does not exist with regard to vaginal plastic operations (Fig. 3). There may be a slightly increased tendency for the patients in the overweight group to lose more blood per operation, but the tendency is not striking. For practical purposes, then, it can be said that the weight of the patient undergoing vaginal surgery does not influence the quantity of blood lost.

From an examination of Fig. 4 it is apparent that the age of the patient undergoing abdominal hysterectomy exerts little influence on the amount of blood lost. The average age in the abdominal hysterectomy series was 45.9 years. Presumably postmenopausal tissues should atrophy and be less elastic and vascular. However, such changes in the tissues did not alter the blood loss during operation.

Fig. 5 shows a definite correlation between the age of the patient and the blood lost during vaginal operations. In the vaginal approach the atrophied tissues which were stretched and scarred with advancing age bled less copiously than those of the younger premenopausal patient. The planes of cleavage were easier to establish and, possibly, the compromised blood supply contributed to the progressive relaxation of the vagina and adjacent structures. Estrogen preparation of the vagina was not made prior to surgery as is the custom in some hospitals, and Pitocin was not injected into the uterus or parametrial tissues of the young patients. The average age of all patients having major vaginal operations was 50.6 years, and the patients in the vaginal hysterectomy series averaged 10 years older than those in the Manchester and anterior and posterior repair groups.

ABDOMINAL HYSTERECTOMY
WEIGHT OF UTERUS (grams x 100)
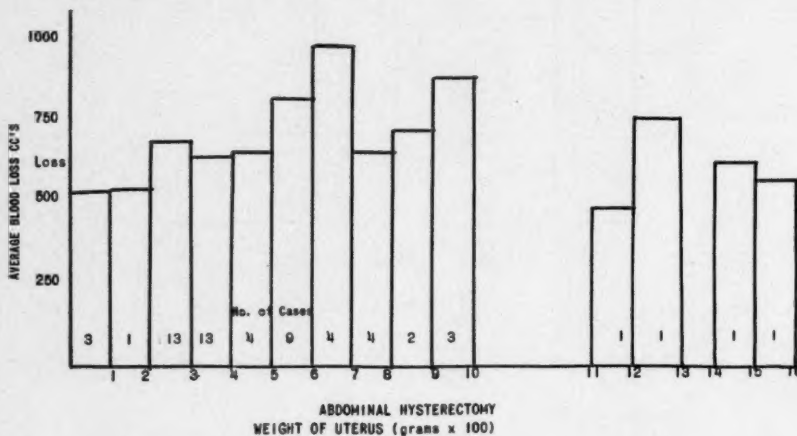
Fig. 6.
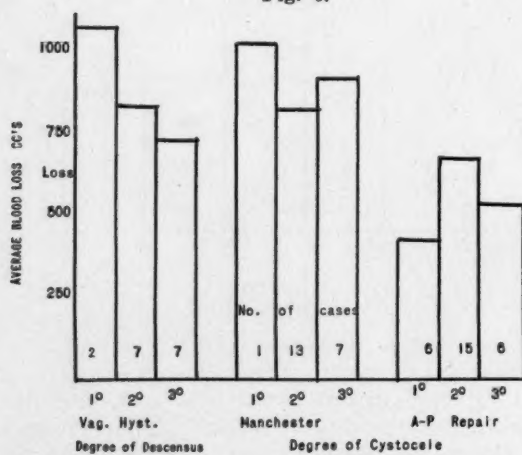
Fig. 7.

It has been considered that a large myoma may signify a difficult procedure, or that a very marked relaxation of the perineum may complicate a standard vaginal repair. Assuming that this is so, the size of the uterus or the degree of relaxation of the perineum should affect the blood loss. Accordingly, the weights of the excised uteri and the degrees of descensus or cystocele were plotted against the blood loss. In neither case was there any consistent indication that the loss was influenced by these factors, for the loss

did not rise with the weight of the uterus, nor did it rise with the increased degree of relaxation of the vaginal outlet (Figs. 6 and 7). Only two patients with a first degree descensus underwent vaginal hysterectomy and, though they distort the graph, they are not significant in altering the over-all picture. Undoubtedly, there are other criteria which one may use to assess the expected ease or difficulty of performing an operation, but these criteria were chosen because they were accessible and had some reasonable pattern of appraisal.

ABDOMINAL HYSTERECTOMY

Loss X Duration of operation

Fig. 8.

VAGINAL PLASTIC OPERATIONS

Loss X Duration of Operations
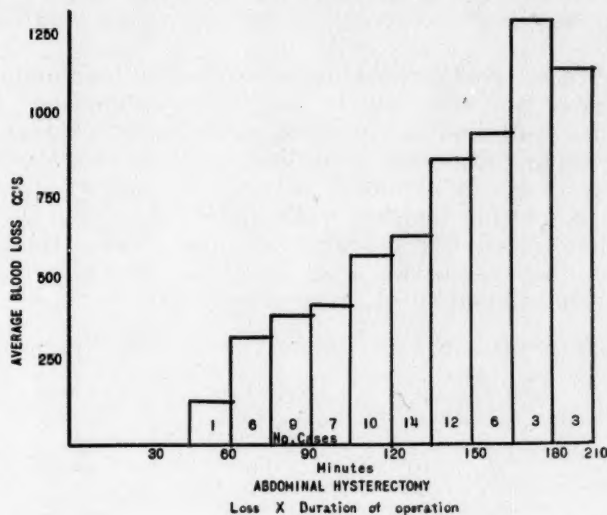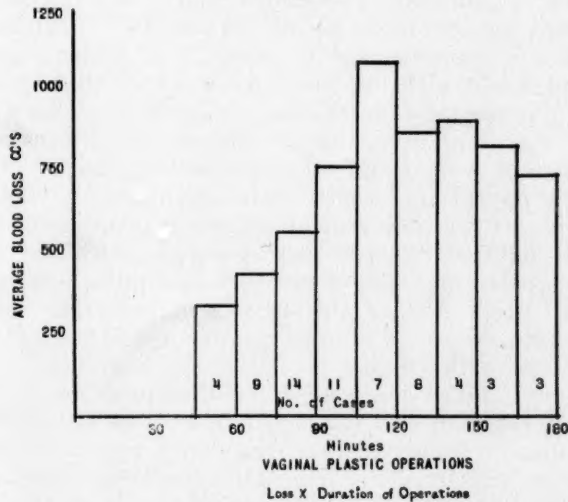
Fig. 9.

Finally, the duration of the operation was studied (Figs. 8 and 9). The longer a surgeon is engaged in dissecting tissue, the greater the blood loss that may be expected. This was true during abdominal hysterectomies and the blood loss increased according to the duration of the operation. In fact, the loci of points fall close to a straight line. However, the vaginal group showed a very interesting variation. A relative limit to the maximum average blood loss occurred after 105 to 120 minutes. The average blood losses from this

point remained fairly uniform. This fact is important, for it makes one realize that blood loss can mount very rapidly and brisk bleeding may herald the approach of shock far sooner than might be expected. It is expedient to begin transfusion early in such cases. The only explanation for this phenomenon that we can offer is that heavy bleeding would stimulate the surgeon to a more rapid completion of the operation, whereas its absence might not demand haste. It should be noted that many operations were done by men on the resident staff who were being trained and taught operative techniques. Accordingly, the time taken to complete the procedure is longer than might otherwise be the case.

At times the necessity of conserving blood may be paramount. Many fine points are considered, and one may be the choice of incision. Blood is lost from the abdominal wall and the question arose as to whether there is any difference in the amount lost with a midline or transverse approach. In the presence of a large tumor or extensive pelvic inflammatory disease most surgeons will choose a midline incision while the Pfannenstiel incision is more suitable for uncomplicated gynecological disease. Table III indicates that there is very little difference between the blood lost with either the transverse or the midline incision, 49 and 40 c.c., respectively.

TABLE III. BLOOD LOSS IN CUBIC CENTIMETERS IN ABDOMINAL INCISIONS

INCISION	NO.	MAXIMUM	MINIMUM	AVERAGE
Midline	26	95	12	40
Transverse	44	146	10	49
Total	70	146	10	46

Some of our cases of carcinoma of the cervix are treated by radical hysterectomy and pelvic lymph node dissections, and it was in this group that the blood loss study paid handsome dividends (Table IV). Ten cases of Stage I and Stage II cervical carcinoma were reviewed, 7 of which received preoperative irradiation, and 3 of which did not. All were treated by extensive Wertheim operations. The average blood loss was 2,340 c.c. with a range between 3,554 c.c. and 1,680 c.c. The operation averaged 314 minutes and about 2,400 c.c. of blood per patient were required to replace the loss. The management of the patient during operation for carcinoma of the cervix was greatly simplified by the institution of the policy of blood loss measurement. When the patient had lost about 200 c.c. transfusion was begun and blood was replaced as it was lost from this point on. Blood pressure and pulse were not relied upon unless hypertension intervened. Caution was exercised to avoid transfusion in excess of the amount lost. Pulmonary edema and atelectasis complicate a long anesthetic, and overreplacement of blood hastens their development and hinders recovery. The patients tolerated the operation and the anesthetic very well under this regimen and it proved to be a most satisfactory method of maintaining a constant blood volume. Sudden drops in blood pressure, vascular collapse, and an overburdened circulatory system were no longer problems as they had been with patients treated prior to this study.

TABLE IV. TEN CASES OF RADICAL HYSTERECTOMY WITH LYMPH NODE DISSECTION

	MAXIMUM	MINIMUM	AVERAGE
Time (minutes)	399	247	314
Blood loss (c.c.)	3,554	1,680	2,340
Blood given (c.c.)	3,500	1,000	2,400

After the patient has left the operating room and returned to the ward the question may arise as to whether or not blood replacement has been ade-

quate. The answer would be easily accessible if blood volumes were determined preoperatively and postoperatively, but the techniques for this procedure are not practical for routine adoption. Other standards of evaluation may be employed in its place and the most common is the determination of the third-day hematocrit or hemoglobin. From time to time, however, the reliability of the hematocrit or hemoglobin has been open to question. Stanton and associates[11] believe that the hematocrit serves as a reliable index of "uncompensated blood loss" but Gatch and Little[4] and Coller and co-workers[12] debate this point. It has been our custom to check the patient's hematocrit on the third postoperative day and because of the variation of opinion its value was investigated.
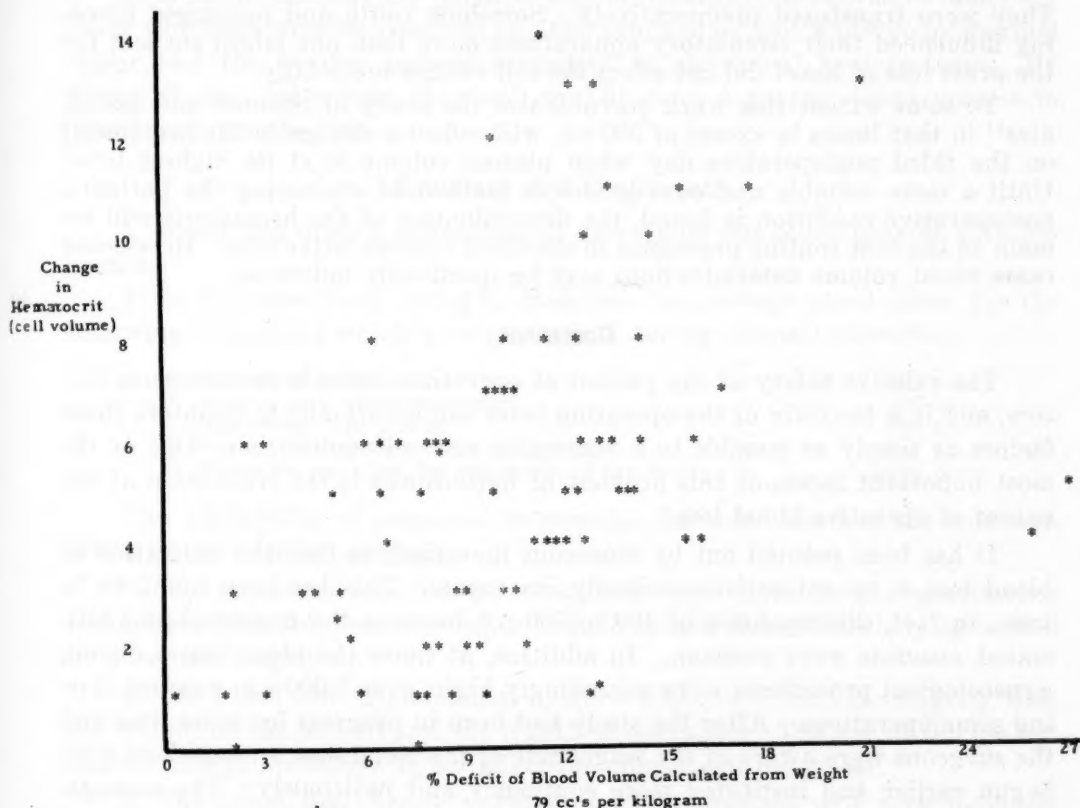
Fig. 10.

An attempt was made to calculate the blood volume from the data in the patient's chart (Fig. 10). The only available point of reference was the patient's weight. Blood volume as a function of the patient's weight is not an ideal figure, but it is satisfactory. We chose to use Dr. Randall's[17] figures based upon several thousand observations. He considers that normal women have 79 c.c.* of blood per kilogram and, if they are over 50 years of age, 10 per cent should be subtracted from the red cell mass. With this in mind the blood volume deficit expressed in per cent was plotted against the change in hematocrit. The blood volume deficit stands for the blood loss divided into the total calculated blood volume, multiplied by 100. In the cases where trans-

*34 c.c. for red cell mass and 45 c.c. for plasma volume.

fusion was used, the blood loss in excess of transfusion was divided into the total calculated blood volume:

$$\frac{\text{Unreplaced blood loss}}{\text{Total blood volume}} \times 100 = \% \text{ Deficit}$$

The scattergraph indicates that not until about a 10 to 12 per cent change in blood volume had occurred did any significant changes take place in the hematocrit determinations between the preoperative and postoperative levels. These changes were not consistent, but hematocrit differences in excess of 6 mm. usually indicate a loss of over 10 per cent in the blood volume. The two patients with 25 per cent deficits were in the fourth decade and had been bleeding heavily for several months before operation from submucous myomas. They were transfused preoperatively. Somehow youth and prolonged bleeding influenced their circulatory apparatuses more than one might suspect for the great loss of blood did not affect the cell volume materially.

To some extent this work corroborates the study of Stanton and associates[11] in that losses in excess of 500 c.c. will reflect a change in the hematocrit on the third postoperative day when plasma volume is at its highest level. Until a more suitable and equally simple method of evaluating the patient's postoperative condition is found, the determination of the hematocrit will remain as the best routine procedure in standard postoperative care. In selected cases blood volume determinations may be specifically indicated.

Comment

The relative safety of the patient at operation depends on numerous factors, and it is the duty of the operating team and anesthetist to maintain these factors as closely as possible to a reasonable state of equilibrium. One of the most important facets of this problem of homeostasis is the realization of the extent of operative blood loss.

It has been pointed out by numerous investigators that the estimation of blood loss at operation is notoriously inaccurate. This has been found to be true; in fact, discrepancies of 400 to 500 c.c. between the measured and estimated amounts were common. In addition, at times the blood losses during gynecological procedures were exceedingly high; over 1,000 c.c. was lost during some operations. After the study had been in progress for some time and the surgeons were aware of the magnitude of the blood loss, transfusions were begun earlier and instituted more cautiously and judiciously. The management of the patient became less complicated. It was a most satisfactory and instructive undertaking. Even if the measurements were to be abandoned now, the knowledge accumulated would be well worth the effort.

Weiner[18] states that "over-loading of the circulation due to transfusion of too much blood or the too rapid injection of blood, particularly in individuals with cardiac disease, is probably one of the most dangerous complications of transfusion, and has been responsible for a number of fatalities." There are times during the dramatic treatment of shock, or the course of a difficult operation, when a surgeon may not be able to assess properly the quantity of blood required for adequate replacement and serious consequences follow. However, if blood loss is measured, the danger of overburdening the circulatory system is reduced to a minimum. Therefore, if radical surgery is

to be utilized in the treatment of carcinoma, and poor-risk patients with a reduced latitude of safety are to undergo surgical therapy, the measurement of blood loss and its satisfactory replacement are invaluable aids to the adequate control.

The determination of the hematocrit on the third day postoperatively, though it does leave something to be desired, will give a rough indication of excessive blood loss. The series is too small to state, however, that in the postoperative period those patients who did not have the deficit corrected did not do as well as those who had adequate transfusions.

It is fortunate that the patients who are destined to lose more blood are those who have greater reserves, i.e., the younger patient undergoing vaginal repair and the heavier patient submitted to abdominal hysterectomy. By virtue of age and weight they will usually have a greater blood volume to compensate for the loss.

Summary and Conclusions

1. Blood loss during gynecological operations was much greater than expected.

2. In the New York Lying-In Hospital, the average blood losses for the following operations which were performed during the past year were:

A. Abdominal hysterectomy	678 c.c.
B. Anterior and posterior repair	556 c.c.
C. Manchester type plastic	849 c.c.
D. Vaginal hysterectomy	716 c.c.
E. Wertheim operation for carcinoma of the cervix	2,340 c.c.

The availability of personnel to measure the blood loss was the only condition in the selection of cases.

3. The measurements for the blood loss were done by the gravimetric technique which has been proved to be both simple and satisfactory by us and by other investigators.

4. The blood loss in abdominal hysterectomies will increase directly with the weight of the patient and the length of operation. The age of the patient and the size of the tumor do not affect the quantity of blood lost.

5. The blood loss during vaginal plastic operations will vary inversely with the age of the patient and directly with the duration of the operation. A maximum average blood loss was reached in 120 minutes and operations which were prolonged beyond this point did not have any greater average blood loss.

6. The degree of vaginal relaxation and the weight of the patient did not alter the blood loss averages during vaginal plastic operations.

7. The blood loss from a transverse abdominal incision is about equal to the loss from a midline incision.

8. One can probably rely upon a third postoperative day hematocrit to reflect a relatively large blood deficit, but it is unreliable unless the loss is in excess of about 12 per cent of the calculated volume by weight.

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THE ISCHIOCAVERNOSUS MUSCLE-SLING PROCEDURE FOR THE CORRECTION OF URINARY STRESS INCONTINENCE*

Preliminary Report

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WHEN one reviews the literature dealing with the operative treatment of urinary stress incontinence in the female, it seems apparent that a paraphrasing of the words expressed by the ancient writer Ecclesiastes[1] is most applicable, when he said, "Of making many books, there is no end; and much studying is a weariness of the flesh." One is now tempted to say, "Of devising new operative procedures for the cure of urinary stress incontinence there is no end; and repeated attempts thereof are a cause of numerous headaches to many gynecologists."

The scope of this paper does not permit a review of all the methods designed for the correction of this disturbing but *not* serious female symptom. Suffice to say that almost every anatomical structure within a reasonable distance of the urethra has been mobilized for urinary sphincteric assistance. Even the urethra itself has been relocated, kinked, twisted, elevated, and freed from adhesions, in the hope of correcting the ailment. So far as can be determined by a diligent search of the American and English literature, the paired striated ischiocavernosus muscles with their covering fascia appear to have been regarded with indifference or neglect in the search for a method of correcting urethral sphincteric weakness under stress.

In the three years occupied in the preparation of this report, the following considerations have been kept in mind. Attempts to correct urinary stress incontinence have not been undertaken without careful preoperative investigation. Such factors have been considered of significance as:

1. The possible inheritance of a defective urethral sphincteric musculature.

2. The possible inheritance of defective urethral and vesical fascial supporting tissues.

3. The .possibility of defective innervation of the bladder and urethral sphincteric mechanism, i.e., as associated with a neurological abnormality.

4. The possibility of irritative lesions of bladder, ureter, and kidney, which tend to produce increased intravesical pressure above the limit of normal urethral sphincteric control.

Urinary stress incontinence not uncommonly may occur with little or no apparent anatomical derangement. There is much diversity of opinion as to

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the actual anatomical or physiological derangement which inherently is responsible for the production of stress incontinence. In fact, all too little is understood about the somatic and autonomic peripheral innervation concerned with the function of urinary control. The scope of this paper, unfortunately, does not permit an elaboration of this point.

Stress incontinence occurs as a common associate of urethrocele; but most commonly, perhaps, it is found in conjunction with some type of genital prolapse such as cystocele, uterine prolapse, enterocele or rectocele. The strain of pregnancy, labor, and/or actual delivery plays undoubtedly the major role in its causation. It is generally accepted, nevertheless, that skillful obstetrical delivery, combined with an adequate episiotomy which is performed prior to marked perineal distention by the presenting part, offers the best hope of prevention of urethral sphincteric weakness.

I first became interested over three years ago in the operative procedure described herein. When some 10 to 12 patients had been operated on with apparently satisfactory results after a follow-up of six months to one year, it was noted for the purpose of record in the 1949-1950 Report of the Dean of Medicine, University of Toronto,[2] that consideration was being given by me to the utilization of the ischiocavernosus muscles in the correction of urinary stress incontinence.

It may be of interest to digress a moment as to the origin of the idea of using the ischiocavernosus muscles as a sling to correct urinary stress incontinence. For many years I had been interested in the work of H. W. Johnston[3] in regard to the surgical treatment of urinary stress incontinence following childbirth. By careful anatomic dissection Johnston was able to prove in such cases definite damage to the external urethral sphincter. It seemed to me that the anterior slinglike portion of the external sphincter was worthy of further investigation. Thus a little exploring was done by carefully channeling forward on each side of the urethra toward the origin of these fibers; then endeavoring to grasp this musculature on each side with an Allis forceps, bring it down, and suture it below the urethral orifice. These fibers of the external sphincter were difficult to locate in sufficient amount to be able to restore adequately the slinglike urethral portion of the sphincter. The proximity of the ischiocavernosus muscles seemed worthy of consideration (Fig. 1). Consequently, I decided to try and fashion a sling from these muscles. It was surprising to note in nearly every case the elasticity of the ischiocavernosus muscles and their overlying fascia. The simple technique described and illustrated herein was very easily developed.

Through the kindness of Professor J. C. B. Grant of the Department of Anatomy of the University of Toronto, the essential safety of the ischiocavernosus sling procedure was indicated by an anatomical dissection; in that the operation does not interfere with either the nerve or blood supply of the displaced portion of the ischiocavernosus muscles. Embryologically the ischiocavernosus muscles, bulbocavernosus muscles, and the external sphincter of the urethra all arise from the same sacral myotomes; and have a common somatic and autonomic peripheral nerve supply.[4] As a result of subsequent ob-

servation of the cases in which the ischiocavernosus sling procedure has been done, an augmentation of the sphincteric mechanism appears to develop as time elapses, suggesting the acquisition of voluntary sphincteric action on the part of the striated ischiocavernosus muscle sling. Voluntary urinary control exercises, but without the use of an intravaginal appliance, as suggested by A. H. Kegel,[5] have been considered an important part of the postoperative advice for one year. In fact, cases presenting minimal postoperative stress incontinence in a few months develop good control through such exercise.
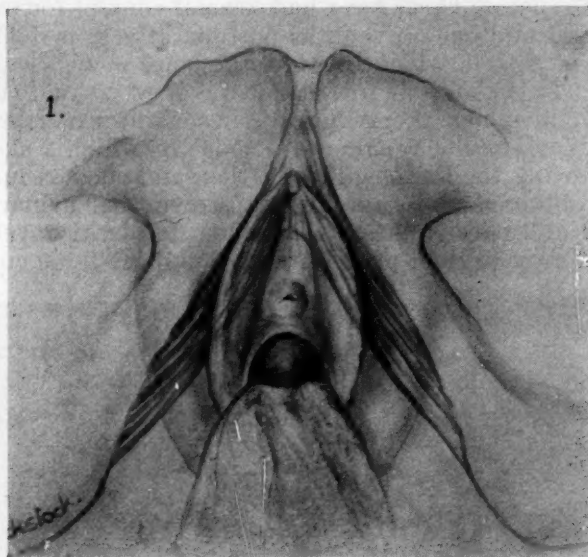
Fig. 1.

Material and Results

In this present report, the first 56 cases operated on are presented. With one exception in this group, the minimum follow-up period has been six months for 6 cases, 8 cases have been observed from 6 months to 1 year, and 42 cases for over 1 year.

Fifty-four of the 56 patients were parous and two were nulliparous. In but 28 of the parous patients was labor stated to be prolonged or difficult. One nulliparous patient had chronic bronchitis for many years, and the other had had a dilatation of a urethral stricture performed by one of the members of the urological service. This was followed by well-marked stress incontinence, presumably indicative of external urethral sphincteric damage.

The youngest patient in this series was 26 years old and the oldest 74. In all but one case the duration of the symptom of stress incontinence exceeded 1 year—the greatest duration was 12 years. Exactly two and one-half times as many patients were over 45 years of age as under 45.

A. Of the total of 56 cases of urinary stress incontinence, in 23 there was either no apparent anatomical derangement, or in conjunction with urethrocele only; however, 7 of this group had associated rectocele and 1 an enterocele. Of these 23 cases, 7 were observed under one year, 12 from one to two years, and 4 over two years. Twenty now appear to be cured, two improved (i.e. with minimum stress incontinence), and one has an unsatisfactory result (this patient having had severe and prolonged postoperative bronchitis).

B. Of the total of 56 cases, in 33 stress incontinence was associated with various forms of genital prolapse. Here the ischiocavernosus sling was performed in conjunction with 16 combined anterior and posterior vaginal repairs; 14 Fothergill operations; 2 vaginal hysterectomies; and 1 Watkins interposition operation. Seven of these were observed under one year, 19 from one to two years, and 7 over two years. Twenty-six now appear to be cured, 6 are improved (with minimal stress incontinence), and one has an unsatisfactory result.

There were 4 cases in which the ischiocavernosus sling had been done as the second attempt to correct stress incontinence following some other primary method of repair. Three have had normal control for over one year and appear to be cured and one six months postoperatively is definitely improved. This is the type of case in which I would like more evidence as to the value of the procedure. Of considerable interest also is the fact that there were 4 cases in the B group (in which the ischiocavernosus sling had been done in conjunction with other vaginal repair operations) of which 2 showed recurrence of cystocele following the Fothergill operation, and one a recurrence of enterocele; but all 4 obtained and have maintained normal urinary control under stress. In the 2 nulliparous patients, in whom the ischiocavernosus sling had been done as the only vaginal procedure, both appear to be cured.
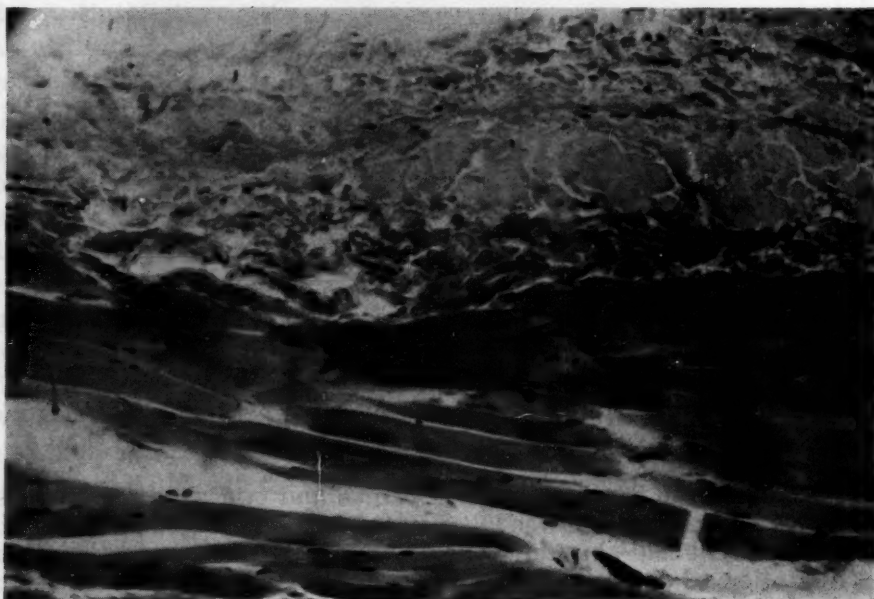
Fig. 1A.

However, let us be frank. It is not my intention to present this ischiocavernosus muscle sling procedure as the answer to every case of urinary stress incontinence in the female. There were two cases (not included in this series) both in patients who were over 60 years of age where the degree of atrophy of the ischiocavernosus muscles was so marked that a sling could not be fashioned. How often one may find this extent of atrophy is not yet determined; but this series contains a group of 13 patients over 60 years of age in whom a sling was possible. Fig. 1A illustrates the point in question, i.e., the presence of partial atrophy in the ischiocavernosus muscle of a patient of 66 years as indicated by loss of striation of some of the muscle fibers.
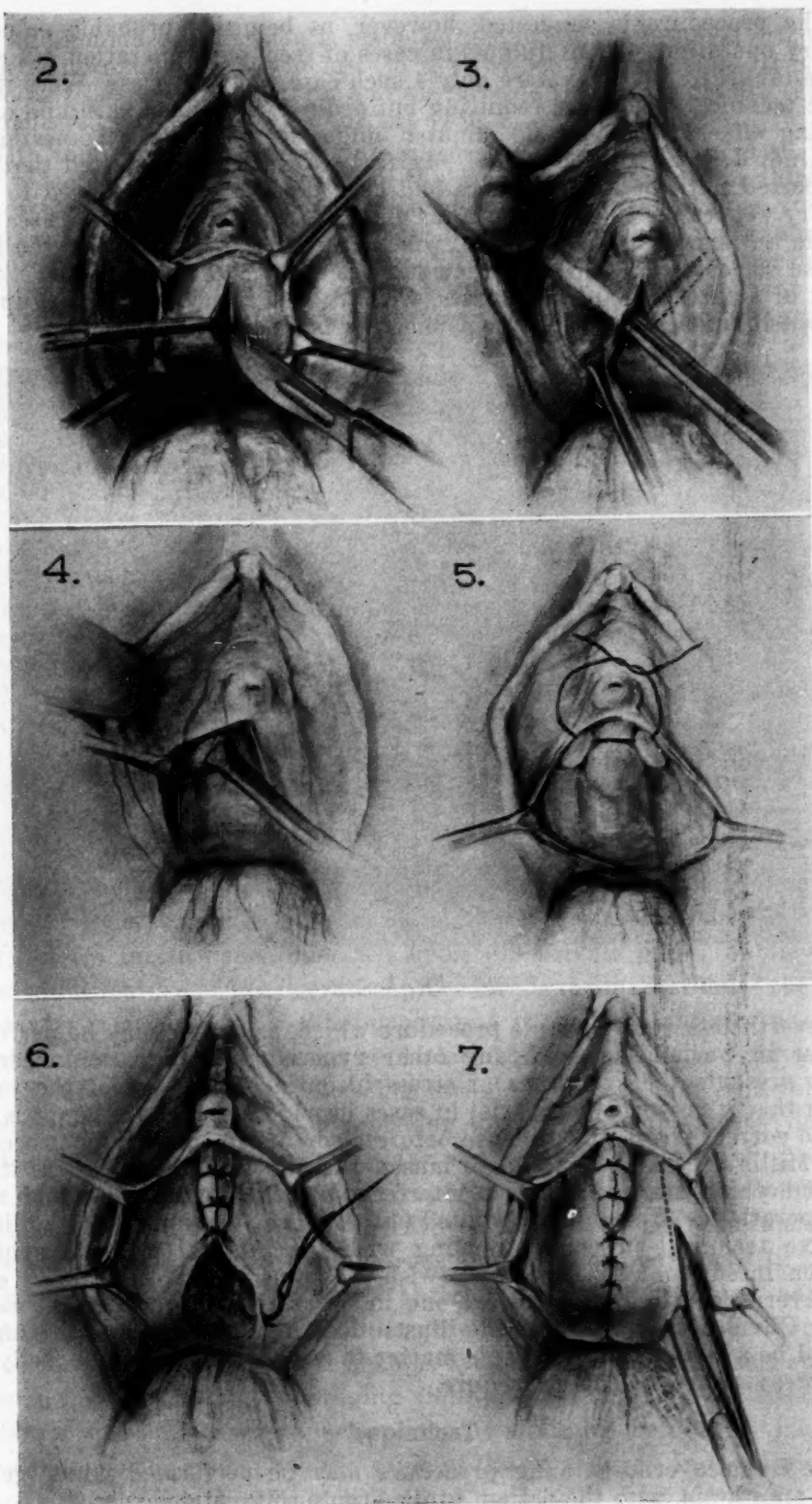
Figs. 2-7.

The procedure is suggested, however, as being of probable value as a
primary operation. Its usefulness in cases of secondary operation has not yet
been established, as there were only 4 such cases in the series. Were it not a
simple technical procedure requiring but ordinary technical skill and capable
of being effected in 20 to 30 minutes, under local or general anesthesia, it
would not deserve to be reported. In fact, I originally requested that it not
be reported until at least 50 cases had been done, and then agreed to a pre-
liminary report on the procedure, as it was my belief that 100 cases might
provide an answer as to its value, whereas it was questionable if the results
of these 56 cases could do more than suggest what might be expected. A later
report of a further 100 to 200 cases, with at least one year's follow-up, must
be awaited before any valid conclusions may be drawn.
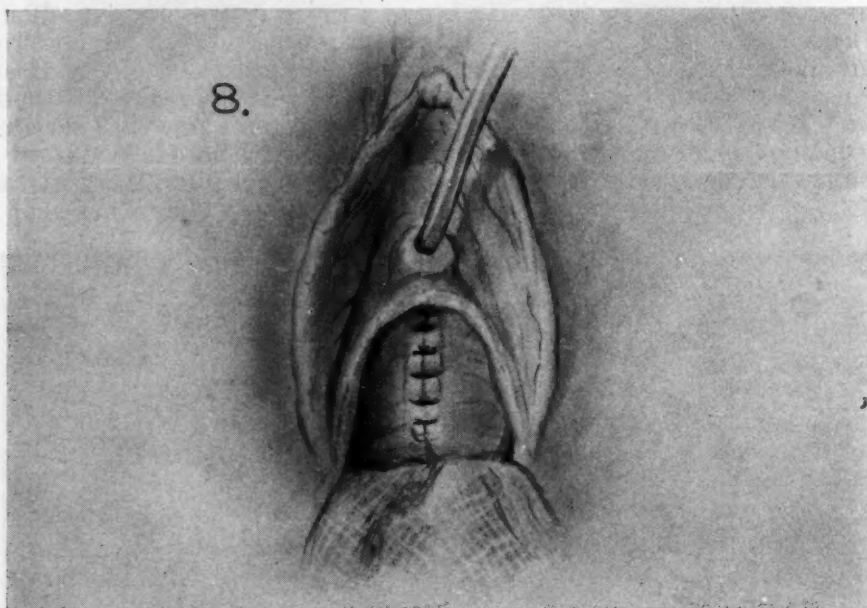
Fig. 8.

Nevertheless, it is a simple procedure which, as stated, may be performed
alone or in conjunction with any other gynecological operation where the
patient presents the symptoms of stress incontinence. I am of the present
opinion that it is worthy of a trial in cases in which a second attempt is to be
made to correct stress incontinence before resorting to such major procedures
as the Millin or some other type of musculofascial or fascial sling. If it fails,
at least nothing has been done to interfere with the technique of such major
sling operations. It should be pointed out that the omission of any additional
operative technical procedure dealing with the internal urethral sphincter
has been intentional, as it was my wish to determine the usefulness of the
ischiocavernosus sling procedure alone in correcting urinary stress inconti-
nence. Obviously, however, as the illustrations of the technique will suggest,
it would be a comparatively simple matter to add, for instance, the Kelly type
of mattress sutures to this procedure.

Technique

The ischiocavernosus sling procedure may be performed under general
or local anesthesia, with the patient in the lithotomy position.

A midline mucosal incision is made ½ inch below the urethral orifice, and extended approximately 1½ inches (in the absence of cystocele). It is deepened so as to expose the urethra, and urethrocele if such is present, the flaps being reflected laterally for this purpose (Fig. 2).

With the use of small dissecting scissors, a channel is made at the depth of the reflected mucosal flaps, toward the junction of the anterior third with the posterior two-thirds of one ischiocavernosus muscle which as stated is located on the inner and anterior surface of the descending pubic ramus. An Allis forceps is inserted into this channel, the muscle grasped and brought to the midline. A similar channel on the opposite side is made at right angles to the first, and the opposite ischiocavernosus muscle is brought to the midline as before (Fig. 3).

Fig. 4 shows the Allis forceps grasping the one ischiocavernosus muscle and its overlying fascia.

Fig. 5 shows the first stitch placed through the displaced portions of the ischiocavernosus muscles, thus creating the beginning of the "sling." This first stitch should bring the anterior part of the sling approximately ½ inch below the urethral orifice. The muscles naturally should be approximated securely but not too tightly, so as to avoid strangulation of tissue. No. 0 chromic catgut has been found to be satisfactory throughout.

Fig. 6 shows the "sling" completed with three stitches. Any laxity in the fascial support of urethra or urethrocele is eliminated with three or four interrupted sutures as shown in Fig. 7.

The redundant vaginal mucosa is excised, and the opening closed with interrupted sutures as shown in Fig. 8.

A 5 c.c. No. 12 Foley catheter is inserted for 4 days for continuous drainage, except for temporary clamping for short periods of ambulation.

Summary and Conclusions

This paper represents the preliminary report of a simple "sling" procedure which has been devised and its use is reported in the first 56 cases of urinary stress incontinence operated upon (49 private and 7 public ward). The essential feature of the operative procedure is the utilization of the paired ischiocavernosus muscles for this purpose. A part of the anterior portion of the belly of each of these muscles is displaced to the midline and sutured just below the urethral orifice. This "sling" would appear to take on a voluntary sphincter effect, augmenting or replacing in function a previously damaged or defective external urethral sphincter. It is possible that marked atrophy of the ischiocavernosus muscles in very elderly patients may preclude this procedure, though atrophy of this extent would appear to be rather uncommon. The series of cases included 2 nulliparous and 54 parous patients. In 23 cases the "sling" was done as the only "anterior" vaginal procedure; and in 33 it was done in conjunction with other vaginal procedures for the correction of some form of genital prolapse such as cystocele, uterine prolapse, etc. The results so far seem to be encouraging and appear to warrant the later report of a larger series of cases. I believe this is advisable before any more conclusive statement is made as to the value of the procedure. In this series there was no death nor any significant morbidity.

I wish to express my appreciation to Professor Douglas E. Cannell for his valued interest in this report, and for his permission to include seven public ward cases in which the operation was performed on the Gynaecological Service of the Toronto General Hospital. To Dr. H. W. Johnston, I am indebted for his generous encouragement to continue with this operative investigation. I am also most grateful to Miss Blackstock of the Department of Art as applied to Medicine, for her excellent illustration of the technique of this operative procedure.

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THE MORBIDITY OF ABDOMINAL HYSTERECTOMY WITH AND WITHOUT PENICILLIN-STREPTOMYCIN VAGINAL SUPPOSITORIES

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SINCE total hysterectomy is to be preferred to the subtotal variety, all available aids to make it as safe a procedure as possible should be provided. Accordingly, in 1948, a standard type of total abdominal hysterectomy was evolved to be used by our staff wherever possible. The technique is very similar to that described by Aldridge.[1] Impressed with the report of Cianfrani and Ziegerman,[2] who showed no difference in the morbidity of hysterectomy with or without preoperative cleansing of the vagina and bolstered by the availability of antibiotics should the need arise, we eliminated preoperative preparation of the vagina from our routine. Recently, the use of an antibiotic in the form of a vaginal suppository has been reported successful in the treatment of both vaginitis[3] and cervicitis.[4] Fletcher[5] reported favorably on the preoperative use of a vaginal suppository containing 100,000 units of penicillin the night before and the morning of operation, including both vaginal and abdominal procedures. Turner[6] reported on 100 consecutive vaginal hysterectomies using a similar suppository, maintaining that the morbidity was reduced from 35 per cent to 7 per cent. In all of the above reports, some form of vaginal cleansing—douching, soap and water washing, or painting with an antiseptic—was used. It seemed necessary to evaluate the effect of an antibiotic suppository in hysterectomy when no vaginal cleansing is employed.

The present report is based on an analysis of 112 consecutive total abdominal hysterectomies, in 48 of which a penicillin-streptomycin vaginal suppository was employed; the remaining 64 served as control cases.

Procedure

The following routine was carried out for the 112 patients in this study, beginning September, 1950, and ending January, 1952: (1) the standard type of operation was performed, (2) the surgery was done by the attending or residency staff, and (3) no attempt was made to select cases.

The suppository-treated group of 48 patients received a vaginal suppository at bedtime the night prior to operation and another inserted immediately following the total hysterectomy.* No other antibiotic was employed.

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*Syncrobin, supplied through the courtesy of the Medical Research Division, Schenley Laboratories, Inc., New York, N. Y., was employed. It contains 200,000 units of penicillin and 200 mg. of streptomycin in a base of 2.1 Gm. cocoa butter and 0.1 Gm. spermaceti.

Results

The data recorded enabled comparison of the morbidity encountered in the 64 control and the 48 treated patients. It is important to note that the two groups were similar in regard to age and major pathology found (Tables I and II). A preliminary series of observations on the effect of the antibiotic suppository on the vaginal flora was also made.

Age.—The average age of the patients in the control group was 42.5 years, ranging from the youngest of 22 to the oldest of 62 years. Likewise, the ages of the treated group varied from 29 to 62 years, with the average being 42.7 years (Table I).

TABLE I. AGE DISTRIBUTION IN YEARS OF 112 PATIENTS HAVING TOTAL HYSTERECTOMY

GROUP	NUMBER OF PATIENTS	YOUNGEST (AGE IN YEARS)	OLDEST (AGE IN YEARS)	AVERAGE AGE
Control	65	22	62	42.5
Suppository	48	29	62	42.7

Major Pathologic Findings.—As noted in Table II, the major pathologic findings in both groups are similar. An attempt was made to compare the most significant diagnosis only. However, in several instances more than one diagnosis was pertinent.

TABLE II. MAJOR PATHOLOGIC FINDINGS IN 112 CONSECUTIVE TOTAL HYSTERECTOMIES

PATHOLOGY	SUPPOSITORY	CONTROL
Fibroids	29	39
Endometrial carcinoma		
Post radium hysterectomy	3	5
Without previous radium	1	0
Noninvasive carcinoma of cervix	2	2
Endometriosis	4	5
Endometrial hyperplasia	6	4
Benign ovarian cysts	2	3
Inflammatory adnexitis	1	2
Tuberculous endometritis	0	1
Cornual pregnancy	0	1
Therapeutic abortion	1	2
Ectopic pregnancy with bilateral		
dermoid cysts	0	1
Chorioadenoma destruens	0	1

Morbidity and Complications.—The standard criterion of 100.4° F. on two days following the first 24 hours postoperatively was used as the basis for reporting morbidity in this series (Table III). There were 17 of the 112 patients who had morbidity, giving an over-all incidence of 15 per cent. This does not include several minor complications which occurred in each group but gave no morbidity. In the main, these consisted of mild respiratory infections and moderate pyuria. There was one instance of failure to void spontaneously for several weeks postoperatively. There was no significant difference in hospital stay between the two groups.

In the control group of 64, 13, or 20 per cent, developed temperature elevations above 100.4° F. If the temperatures caused by wound hematoma or wound serum collection, respiratory infection, pyuria, or faulty surgery are discounted because vaginal preparation would not be a factor in their causation, 4 instances of morbidity still remain. Of these, 2 had vaginal cuff infections and the remaining 2 had no determinable etiological factor.

The study group of 48 patients who received a vaginal suppository pre- and postoperatively according to the routine described above had a lower morbidity than observed in the control group (Table III). Only 4 patients developed postoperative fever, giving an uncorrected morbidity of 8 per cent. However, excluding Cases 1 and 2 on the basis that wound hematoma and pyuria are not pertinent to this study, only two unexplained elevations remain. In neither case was the temperature severe or the duration more than 48 hours. No cuff infections were noted in the treated group.

TABLE III. MORBIDITY IN 112 PATIENTS AFTER TOTAL ABDOMINAL HYSTERECTOMY

NO.	HIGHEST TEMP. DEGREES F.	DAYS POSTOPERATIVE	ETIOLOGICAL FACTOR
Control.—			
1	102	2-4	Hematoma of right parametrial region
2	101	5-6	Respiratory infection
3	101	2-6	Serum collection in wound
4	101	6-10	Pelvic peritonitis with cuff infection
5	101	6-12	Vesicovaginal fistula
6	101	6-7	None found
7	101	2-3	Pyuria
8	103	2-6	Wound infection
9	102	1-8	Vaginal cuff infection
10	101	1-4	None found
11	101	2-11	Pyuria—patient diabetic—postoperative irradiation for endometrial carcinoma which had invaded the pelvis
12	102	2-10	Severed ureter with primary anastomosis and subsequent cutaneous ureterostomy
13	103	2-3	Respiratory infection
Suppository.—			
1	103	3-6	Wound hematoma with infection
2	102	2-3	Pyuria
3	102	2-3	None found
4	101	2-3	None found

Vaginal Flora.—It has been shown, by means of preoperative and fourteen-hour postoperative cultures, that a penicillin vaginal suppository inhibits the growth of pyogenic cocci.[6] For that reason, it was felt that it would be of value to determine if the suppository used in the present study, which contains not only penicillin but also streptomycin, exerted any persistent effect on the normal vaginal flora. Accordingly, only those patients who had a normal flora preoperatively and who received no other antibiotic pre- or postoperatively, which could possibly influence a culture of the vaginal flora, were observed for this purpose. Aerobic and 10 per cent carbon dioxide cultures were performed using broth and blood agar plates with a brain-heart infusion base for each. Although 20 patients were studied by means of vaginal culture, only 6 met the above requirements. In each of the 6 patients, the preoperative culture was taken immediately before inserting the suppository. All preoperative cultures showed rodlike organisms, probably the Döderlein bacillus; 4 of the patients also had *Staphylococcus albus.* Cultures were repeated on the fifth postoperative day. All of the postoperative cultures showed both rodlike organisms, probably the Döderlein bacillus and *Staph. albus.* Though this is a preliminary report on a small number of cases, the uniformity of the

findings permits the presumption that the suppository employed does not significantly alter the normal vaginal flora. Further investigation of this problem is needed.

Comment

It is fully realized that the 112 patients analyzed do not constitute a sufficiently large group to be statistically valid. However, it is felt that the observations are clinically significant and are instructive. One can readily see the apparent decrease of morbidity in the group in which the suppository was employed. In addition, the consistent finding of normal flora five days postoperatively permits us to presume that the vaginal flora is not significantly altered by the use of the suppository. There was no instance of sensitivity in the entire treated group. An additional observation of interest was the fact that at operation no remnant of the suppository inserted vaginally the night prior was found.

Any new procedure must not only be effective but also relatively simple. Certainly the insertion of a suppository into the vagina pre- and postoperatively is neither difficult nor time consuming. On the basis of our experience, as well as that of others,[5, 6] it may be concluded that an antibiotic vaginal suppository is effective in decreasing the postoperative morbidity and complications of total abdominal hysterectomy. These separate observations may not be valid individually but certainly appear impressive in the light of their uniformity. For this reason, the routine for total abdominal hysterectomy at our hospital has been revised to include the insertion of an antibiotic vaginal suppository pre- and postoperatively.

Summary

1. The effect of a streptomycin-penicillin vaginal suppository upon the postoperative course of patients subjected to total abdominal hysterectomy was analyzed.

2. The suppository was employed pre- and immediately postoperatively in 48 patients; 64 additional patients received no suppositories and served as controls.

3. No sensitivity, local or systemic, to the suppository was encountered. The suppository was observed to melt and to be absorbed readily.

4. A decrease in morbidity was observed in the treated group.

5. Normal vaginal flora was not significantly altered in 6 patients subjected to repeated vaginal cultures.

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IS PREGNANCY FOLLOWED BY RELATIVE HYPOTHYROIDISM?*

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IN HUMAN subjects pregnancy is characteristically accompanied by increases in serum protein-bound iodine and thyroxine.[1-3] Following delivery at term the protein-bound iodine decreases rapidly, but no extensive data are available as to what levels can be expected in the postpartum period.[3, 4] This study indicates that a return to or below the range of concentrations encountered in nonpregnant adult women occurs in several weeks, but that unduly low values may be present for at least a year following gestation.

Material, Methods, and Results

Blood has been withdrawn from 95 women patients, 1 to 52 weeks after delivery in uncomplicated pregnancies, and analyzed for serum protein-bound iodine.[5, 6] The findings have been compared with those obtained in a series of young women in the last trimester of pregnancy as well as with those in young adult women in the same age and social groups, but without a history of pregnancy. From Fig. 1 it is readily evident that uncomplicated pregnancy is usually accompanied by marked elevations and fluctuations in the serum protein-bound iodine. The latter may be as great as 2 or 3 gamma per cent or more from month to month. However, even when this instability is taken into account, the mean values for this group of patients is still clearly in excess of the average (5.44 ± 0.82) in a group of 125 sera from nonpregnant adults in the same age group. There is no evidence of a trend either upward or downward during any of the months of the last trimester (7.53 ± 1.45, 7.19 ± 1.55, 7.77 ± 1.57, respectively) nor are the values noticeably different at the time of, or shortly after, parturition (7.08 ± 1.55).

In Fig. 2 it can be seen that the iodine values decline following delivery. A few sporadic increases reminiscent of fluctuations present in the prepartal pattern may be encountered, but by the fifth week and probably earlier most of the values have returned to the euthyroid range. From Fig. 2 it is further evident that individuals with a recent history of pregnancy have protein-bound iodine values which are significantly lower. Thus, in sera obtained between the fifth and eighth weeks post partum the mean protein-bound iodine was 4.65 ± 0.88 gamma per cent. This level is distinctly lower than that characteristic of the control group, 5.44 ± 0.82. This statistically significant depression of the iodine value is still apparent in samples obtained during the ninth to twenty-fifth, as well as during the twenty-sixth to fifty-second, week following

delivery. The limited data do not permit definitive statements as to whether the low iodine values occur any more often in those mothers who nurse their infants, nor in those in whom normal menstruation had not returned.
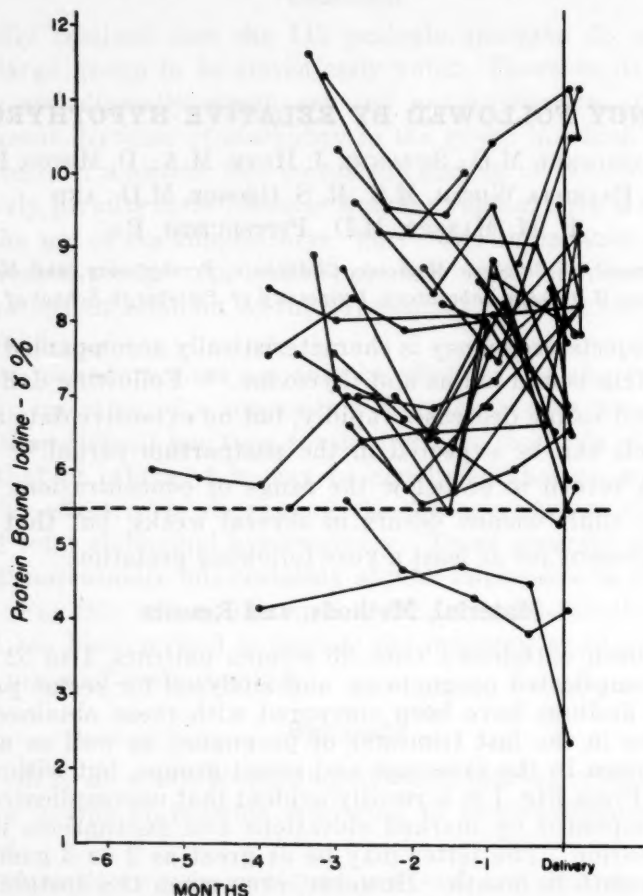
Fig. 1.—Protein-bound iodine values in pregnant and nonpregnant women.

The dotted horizontal line refers to the mean protein-bound iodine value (5.44 ± 0.82) obtained in a series of 126 sera from healthy young women without a history of pregnancy. The interconnected points indicate the successive levels of protein-bound iodine in young women in the last trimester of uncomplicated pregnancies. In the latter group the protein-bound iodine levels during the seventh, eighth, and ninth months (7.53 ± 1.45, 7.19 ± 1.55, and 7.77 ± 1.57 gamma per cent) are statistically significantly higher and show fluctuations which are greater than those characteristic of the control group.

Comment

It is possible that this lower mean postpartum iodine value indicates a depressed level of thyroid activity in at least some of the women included in this study. Such a state of relative hypothyroidism could account for a portion of the nonspecific postpartum complaints ordinarily attributed to increased maternal and household burdens. A definitive statement cannot be made because (a) no substantial number of prepregnancy iodine values are available in this group of subjects, (b) it has not been established that variations within the euthyroid range necessarily reflect altered levels of thyroid activity, and (c) the effects of desiccated thyroid administration in these patients have not been defined. On the other hand it is known that serum protein-bound iodine levels do accurately reflect hypo- and hyperthyroidism[7, 8]

and that healthy young adults do not show such downward shifts in protein-bound iodine when studied during periods of several months[9] and indeed even when examined at intervals of one or more years.[10] The possibility that the low mean values are attributable to alterations in serum or plasma proteins[11] seems unlikely in view of the repeated demonstrations, chemical and electrophoretic, that within 6 to 12 weeks of delivery the protein fractions have returned to values and patterns characteristic of nonpregnant adults.[12-14]
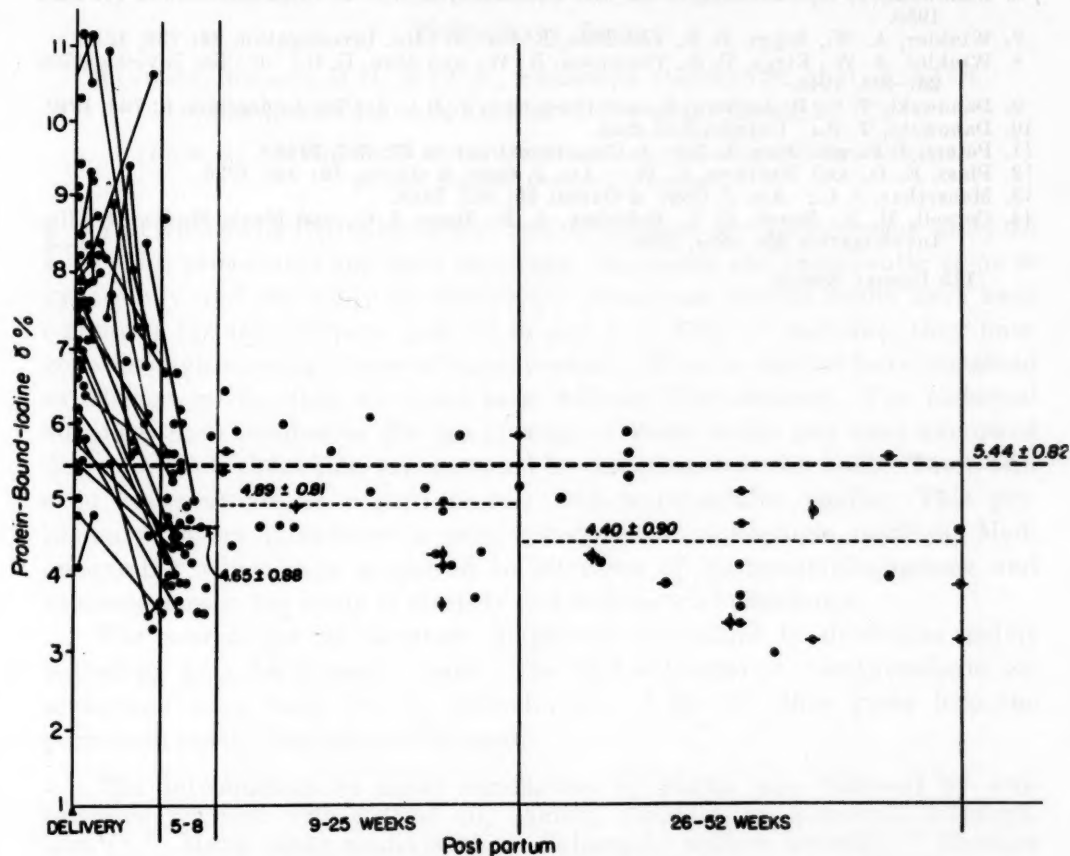
Fig. 2.—Protein-bound iodine at the time of and after delivery.

The horizontal bar superimposed on a solid circle identifies mothers who were nursing their infants at the time serum was obtained; the vertical line indicates that normal menstruation had not returned. By the fifth to the eighth week post partum, or earlier, the mean values, 4.65 ± 0.88, are below that characteristic of young adult women without a history of pregnancy, 5.44 ± 0.82. This statistically significant difference is still present one-half and even one year following delivery as indicated by the average concentrations obtained during the ninth to twenty-fifth, and twenty-sixth to fifty-second weeks post partum, 4.89 ± 0.81 and 4.40 ± 0.90 gamma per cent, respectively. In these three comparisons with the control subjects "p" values of 0.002 or less were obtained.

Summary

The finding of lower serum protein-bound iodine values during the first year post partum raises the possibility that an interval of relative hypothyroidism follows upon normal pregnancy.

Addendum

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125 DESOTA STREET

A NEW WATER-SOLUBLE OPAQUE MEDIUM IN THE STUDY OF HYSTEROGRAMS AND HYSTEROSALPINGOGRAMS

Preliminary Report

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HYSTEROSALPINGOGRAPHY and hysterography have become accepted office procedures and have important diagnostic and therapeutic value in gynecology and the study of infertility. Numerous opaque media have been employed for this purpose and, as in any new field of medicine, they have gone through varying stages of improvement. While a number have remained as efficient media, they have not been without shortcomings. The technical advances have eliminated the use of some of these media and have narrowed down to a few those that are accepted by technicians in the field. There still exist controversies in regard to oily and water-soluble media. This preliminary report introduces a new water-soluble radiopaque medium, Medopaque-H,* which was employed in 50 cases of hysterosalpingograms and hysterograms in the study of sterility and endometrial pathology.

The search for an accurate diagnostic procedure to determine pelvic pathology goes back many years. The first attempts at roentgenologic observations were made by the introduction of air or other gases into the peritoneal cavity (pneumoperitoneum).

The introduction of tubal insufflation by Rubin was followed by considerable research with iodized oil, namely, Lipiodol, by numerous investigators.[1, 2, 3] Many other media such as Collargol,[4] sodium bromide,[5, 6] thorium citrate,[5] and bismuth paste had all been previously used but were found unsatisfactory.

In 1926, Lipiodol was first used in the study of tubal obstruction, tubal peristalsis and sterility.[2, 7-11] Since then other opaque media that have been made available include Lipoiodine, Contrastol, Brominol, Iodochlorol and Umbrenal, thorium dioxide, iodomethane sulfonate (Skiodan) in acacia, and Visco-Rayopake.

As early as 1933, Neustadter recognized the need for a harmless radiopaque medium when he offered the following requirements: (1) The ideal radiographic medium must be totally innocuous to the organism as well as to the reproductive organs. (2) It must possess that degree of resorbability which shall enable it to disappear from the system rapidly and completely after it has accomplished its diagnostic purpose, leaving no residue. (3) It must have the proper viscosity that will adequately permit of radiographic demonstration of adherent and partially strictured tubes.

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*Supplied by Bell-Craig, Inc., New York, N. Y.

In the attempt to produce a substance of proper viscosity that provides good contrast, is nonirritating to living tissue, and has quick absorbability, the radiopaque medium Medopaque-H may fulfill these requirements. It has advantages over some of the other media since it is absorbed within one hour, thus avoiding any possible peritoneal irritation or formation of granulomatous lesions. Encouraging work with this medium is also being reported in the field of urology (Medopaque-U).[12]

Medopaque-H contains the compounds sodium ortho-iodohippurate as contrast agent, sodium carboxymethylcellulose (CMC) as the viscosity vehicle, with added stabilizer and preservatives. The complete formula is as follows:

Sodium ortho-iodohippurate	45.0 %
Carboxymethylcellulose (CMC)	1.83%
Sodium citrate	0.4 %
Methyl paraben	0.18%
Propyl paraben	0.02%
Viscosity in centistokes	250

Sodium ortho-iodohippurate was first reported by Swick.[13] It is a halogen derivative of a compound (hippuric acid) normally found in the human urine as a detoxification product. It is a white crystalline powder, very soluble in water, containing about 35 per cent iodine in stable organic combination. It is one of the least toxic organic iodine compounds, rapidly absorbed and well tolerated orally and intravenously.

Sodium carboxymethylcellulose (CMC, a viscosity-increasing substance) is the sodium salt of carboxymethylcellulose or cellulose glycolic acid. It is a cellulose ether made by the reaction of monochloracetic acid with alkali cellulose. CMC is a white, fluffy, hygroscopic solid, easily soluble in water, forming viscous solutions in concentrations of about 3 per cent and a gel at 5 per cent concentration. It is nonirritating and harmless physiologically to skin, mucosa, and external genitals.[14, 15]

After experimenting with various viscous preparations, Morales and Heiwinkel[16] found that sodium carboxymethylcellulose met their demands. They had been searching for a viscous contrast medium that was not only soluble in water but which could be easily resorbed, a feature not attributable to the iodized oils. It had to be nonirritative and sufficiently stable to endure sterilization and storing. After administering CMC to dogs and rats per os, Brown and Houghton,[14] and Werle[17] reported normal postmortem examinations of the vital organs. Shelanski and Clark's work[18] confirmed this and these authors concluded that CMC showed no evidence of toxicity to experimental animals or human beings. They also used CMC in powder form as a vehicle for an antiseptic substance in 134 cases treated for vaginal infections and there were no untoward reactions—and no evidence of infection of the vaginal mucosa or external genitals.

Morales and Heiwinkel[16] confirmed these findings by using CMC with other media. Further studies by Morales[19] reconfirmed the original use of CMC, also finding that the surface tension was relatively low. It therefore spreads rapidly and covers large surfaces.

Many and varied untoward reactions have been reported with the use of the iodized oils. In several cases, Robins and Shapira[20] noted a small amount of this medium under one diaphragm. In the presence of pelvic adhesions, the iodized oil may be collected into several small pools behind the uterus or in the regions of the distal portions of the tubes. These small collections may become encysted and remain for months and years with little evidence of absorption. They remain as inert foreign bodies. The same phenomenon was observed in occluded tubes. It is possible that a hydrosalpinx may become overdistended by oil and rupture thus occur.

The number of infections and inflammatory reactions occurring after the use of iodized oils also militates against the use of these preparations. Rubin[21] stresses that the injection of iodized oils into the uterus often causes untoward effects due to retention of oil and its slow rate of absorption. In the absence of infection, the oil thus retained acts as a chemical irritant. He has also noted that the myometrium and parametrium are at times infiltrated by iodized oil when the latter is injected under high pressures and, because of slow absorption, an inflammatory reaction may occur.

Gauss[22] reported 3,000 cases in which the incidence of infection was 1 in 230. Schultze[23] had an incidence of 1 in 300 among 8,000 cases, but believes his figure is not accurate since all complications are not reported. He states that experience has shown that even with careful selection of cases and careful technique, there can be no absolute guarantee against inflammatory complications and believes his figure should be about 1 in every 100 cases.

Fig. 1.—Initial flat plate of the pelvis to rule out any opacity prior to the instillation of Medopaque-H.

Material and Method

Medopaque-H was used in 50 infertility cases from the Infertility Clinic and Department of Gynecology of the Queens General Hospital. Five of the 50 cases were for endometrial studies and 45 for tubal patency.

The technique was as follows:

An initial x-ray plate of the pelvis was taken to determine the presence or absence of any opacities before the opaque medium was injected. The usual time for hysterosalpingography was four to six days after cessation of the menstrual period (Fig. 1).

A Bakelite speculum was used that would not show up on the x-ray film. The cervix was prepared with antiseptic and the anterior lip grasped with a tenaculum. The Jarcho cannula, which had been previously filled with Medopaque-H, was inserted into the cervical canal and a tight fitting obtained. A 10 c.c. Luer-Lok syringe was used to inject 2 c.c. of the medium into the

uterine cavity and an x-ray plate then taken (Fig. 2). This same procedure
was repeated and fractional x-ray films were taken after each 2 c.c. instillation
until a total of 6 c.c. of the Medopaque-H had been introduced (Figs. 3 and 4).

Fig. 2.—X-ray plate of the pelvis after instillation of 2 c.c. of Medopaque-H. The uterine
cavity and cervical canal can be noted and both tubes are outlined almost to their distal ends.
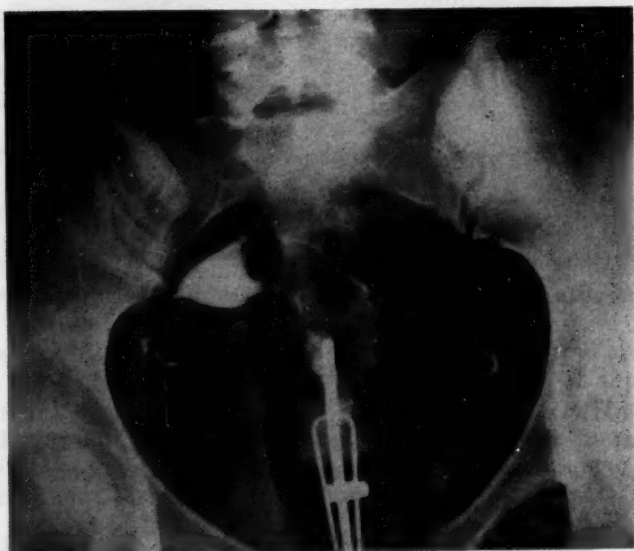
Fig. 3.—X-ray plate of the pelvis after a total of 4 c.c. of Medopaque-H has been instilled. The
opaque medium can be seen at the fimbriated end.

At this time, the tubal insufflation apparatus was connected to the inserted
cannula and carbon dioxide was permitted to force the Medopaque-H through
the Fallopian tubes. The pressure was never allowed to go above 200 mm. Hg.
After one minute of sustained pressure at 200 mm. Hg, or lower, depending
upon the case, another x-ray plate was taken and the plates developed (Fig.

5). If the opaque medium was found in the peritoneal cavity, the procedure was concluded; if not, the pressure was continued for several minutes more and another plate taken. If this latter procedure failed to establish patency, the point of obstruction was noted and the patient subjected to pelvic diathermy with a repeat of the hysterosalpingogram after two months.
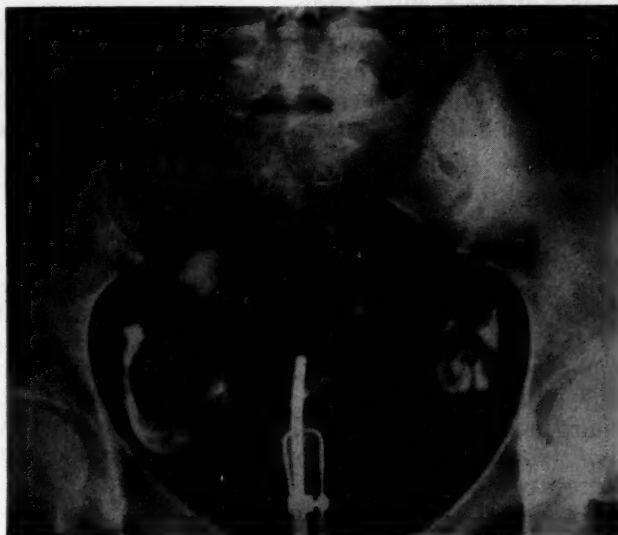
Fig. 4.—X-ray plate of the pelvis after instillation of 6 c.c. of Medopaque-H followed by some carbon dioxide. The opaque medium can be seen free in the pelvic cavity.
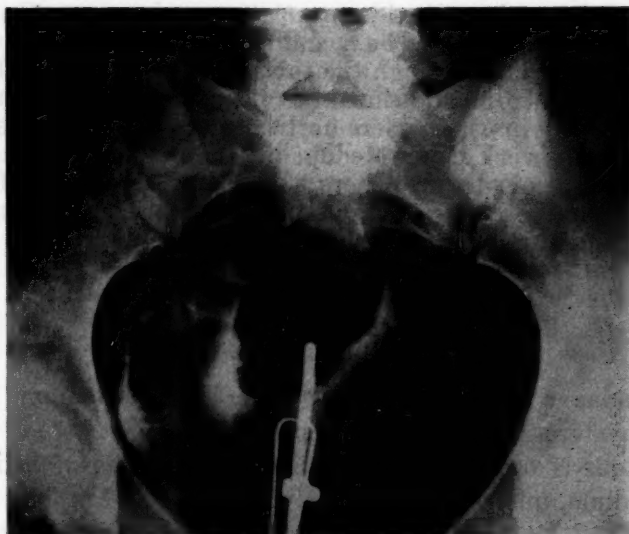
Fig. 5.—X-ray plate of the pelvis after insufflation of carbon dioxide for 2 minutes under sustained pressure of 200 mm. Hg. Note that the medium has left the uterine cavity and has been distributed in the pelvic cavity.

For those cases in which the examination was made to determine endometrial pathology, the procedure was confined to the fractional method using Medopaque-H alone.

Results

Of the 45 cases for hysterosalpingograms, 25 showed patency on the first attempt with Medopaque-H and carbon dioxide insufflation. The remaining 20 cases showed obstruction or occlusion as follows:

> 8 cases at the fimbriated ends
> 10 cases at the cornual ends
> 2 cases at the mid-portion of the Fallopian tubes

In 6 of the 8 cases with obstruction at the fimbriated ends, patency was established after two to four repeat hysterosalpingograms and pelvic diathermy. Only one tube with obstruction at the cornual end could be made patent. Patency was not established in either of the mid-portion cases.

Comment

This preliminary report on the use of a new opaque medium, Medopaque-H, is presented because of its encouraging results in hysterosalpingography. The outstanding feature of this medium is its remarkably rapid absorption with no residue, thus eliminating the danger of the formation of granulomatous lesions, pelvic adhesions, and irritating foci, as have been reported with oily media. One hour after the instillation of Medopaque-H, no traces could be demonstrated roentgenographically anywhere in the pelvic cavity. While Medopaque-H does not provide as sharp a contrast as iodized oil, we believe that it is sufficient to demonstrate the pathology.

Although the series of cases presented is relatively small, this new medium has been found to be efficient, innocuous, and nonirritating. Its only disadvantage, as is true of other water-soluble media, is that a 24 hour plate cannot be obtained. However, our technique for hysterosalpingography as described by others has been modified and the combination of the opaque medium followed by carbon dioxide insufflation under controlled pressure has been found very satisfactory. The sustained pressure of carbon dioxide that forces the opaque medium through the tube is of great value. The use of this combined technique has the additional advantage of being a therapeutic measure as well, especially in cases where obstruction is found on the first attempt.

The preliminary work using Medopaque-H in hysterosalpingography also confirms the findings of other workers, i.e., obstruction at the fimbriated end of the Fallopian tube is more amenable to being made patent than that at the cornual end or mid-portion. In the near future, we hope to be able to report on a much greater series of comparative studies with various media in conjunction with the infertility problems at the clinic of Queens General Hospital.

Summary

1. A preliminary study with a new water-soluble medium, Medopaque-H, in 50 cases of hysterosalpingography is presented.

2. Medopaque-H appears to meet the requirements of being a harmless radiopaque medium, innocuous to the pelvic organs, and rapidly absorbed.

3. A combined technique for hysterosalpingography, using fractional instillations of Medopaque-H followed by carbon dioxide insufflation, is described, thus eliminating need for a 24 hour plate.

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HEMORRHAGIC DIATHESIS IN ABRUPTIO PLACENTAE*

With Particular Reference to the Indications for Cesarean Section

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ALTHOUGH the commonly accepted definition of abruptio placentae is any appreciable detachment of the normally implanted placenta occurring between the twenty-seventh week of pregnancy and the third stage of labor, our experience has shown us that this accident can occur as early as the twenty-third week and that these cases should be treated like other cases of abruption. The treatment of any woman having abruption of the placenta is dependent upon the severity of her condition.

Cases of abruptio placentae have been clinically classified by McCord,[1] Gustafson,[2] and others, as mild, moderate, and severe, according to the severity of the constitutional manifestations. The mild cases are those in which there are no symptoms nor signs other than slight vaginal bleeding; they require no special treatment, usually deliver themselves rapidly, and are generally diagnosed only in retrospect, after inspection of the recently delivered placenta shows fresh, adherent blood clot over a marginal portion of the maternal surface. In the moderate cases there might be slight hypertonicity of the uterus and moderate vaginal bleeding, with mild or no shock. These are best treated conservatively and delivered through the pelvis, which is usually readily accomplished since most are already in labor. The severe cases are those in which there is shock, the uterus is tender, distended, and of boardlike consistency, and no fetal heart sounds can usually be heard.

The management of these cases of abruptio placentae, particularly the severe cases, is the chief concern of this paper, since the maternal mortality in the severe group is from zero per cent[2] to approximately 20 per cent,[3] and the fetal mortality is about 100 per cent. Concerning the causes of maternal death, Kellogg,[4] in reporting on the cases of abruptio placentae at the Boston Lying-in Hospital, showed that no deaths in the group treated by cesarean section were due to hemorrhage, or "hemorrhagic diathesis," while more than half of those of the vaginal delivery group who died did so from hemorrhage. We have construed these facts as indicating that the time factor, from the onset of abruption to delivery, enters into the production of the spontaneous or excessive bleeding state, hemorrhagic diathesis.

How great a threat is hemorrhagic diathesis in patients having abruptio placentae? It is said to be found chiefly in the severe cases, and Kellogg[5] reported eight women who had an excessive bleeding tendency in an illustrative series of 23 cases which represented varying types of abruption. We have studied this aspect of abruptio placentae by doing quantitative fibrinogen tests (method of Ware, Guest, and Seegers[6]) on the plasma from samples of blood drawn from 10 cases of placental abruption before, at the time of, and/or following delivery. The 10 cases studied were the more severe ones selected from a total of 23 cases which occurred during an aggregate period of 1,986 deliveries, an incidence of 1.2 per cent. The results of our studies are shown in Table I, and the two main facts that they establish are: (1) the defibrination tends to continue until delivery, and (2) following delivery the fibrinogen levels rise toward normal. The significance of these facts is that the abruption state is the cause of the defibrination, since delivery, by emptying the uterus of its pregnancy, chiefly accomplishes interruption and abolition of this state. It has been fairly well established that the hemorrhagic state which occasionally occurs in moderate and severe cases of abruptio placentae is due to the depletion of the fibrinogen[7, 8, 9, 12] and our findings (Table I) further substantiate this belief. The depletion of the fibrinogen, in turn, we believe to be due to liberation of thromboplastin into the maternal blood stream from tissues at the abruption site.[7]

General Consideration of the Fibrinogen Levels

Since we found in our controls that the fibrinogen levels are about 325-400 mg. per cent in the average woman at time of delivery, it is readily apparent in Table I that in the two mild cases of abruption there was no actual defibrination of the blood. In these cases there was only slight intrapartum vaginal bleeding and the fresh placenta subsequently showed separation of about one-fourth of its surface following rupture of a marginal sinus.

In the four moderately severe cases (Table I) we find a wide variation between their relative degrees of defibrination, these values for plasma fibrinogen being, respectively, 57, 2, 27, and 9 per cent of normal, the last three values being found in cases evidencing some hemorrhagic diathesis. In Case M. C. the uterus had to be packed and repacked before the blood transfusion and the patient's own resources (probably principally the liver) supplied sufficient coagulation agents to correct the disruption of the blood-clotting mechanism. Case B. H. had excessive vaginal bleeding immediately post partum for a short time, but it was quickly checked with the usual measures and the administration of blood. The bleeding in this case probably was not evidence of a real hemorrhagic diathesis. Case E. L. bled from the uterus and from the repaired perineal laceration for one hour following delivery, after which her clotting mechanism recovered, again on the basis of the transfusion of fresh, whole, citrated blood as well as her own resources.

In the four severe cases in Table I we note real degrees of defibrination, but none as great as in two of the cases in the moderate group. Three of these four cases had real hemorrhagic diathesis. Case P. M. required 2,500 c.c. of blood just before and during the cesarean section performed upon her, and she bled from every suture placed in the uterine and abdominal incisions, but,

TABLE I. CONCENTRATIONS OF FIBRINOGEN, IN MILLIGRAMS PER CENT, IN THE PLASMA OF 10 WOMEN* DURING ABRUPTION OF THE PLACENTA AND FOLLOWING EMPTYING OF THE UTERUS

| CASES | TIME AFTER OCCURRENCE OF PLACENTAL ABRUPTION | | | | | | | | | | | | | | | | CLINICAL HEMORRHAGIC DIATHESIS |
| | NUMBER OF HOURS | | | | | | | | | NUMBER OF DAYS | | | | | | | |
	2	4	6	8	10	12	14	20	22	2	3	4	5	6	7	8	
Mild.—																	
M. S. HKH No. 112394	331		402			Del.†									447		No
E. B. HKH No. 98573								Del.		254	257	244	282				No
Moderately Severe.—																	
H. D. HKH No. 106744			320				Del.† 1T		250	400	440		390				No
M. C. HKH No. 117359					Del. 10	150	200 1T										Yes (uterus packed twice)
B. H. HKH No. 117626			Del. 120 1T							213	1T						No
E. L. HKH No. 111278	38	Del. 56 1T				1T			238	294	384	348		1T		515	Yes (for 1 hour)
Severe.—																	
P. M. HKH No. 105006		90	2T	Sec.† 1T	2T					2T	440 2T	520				540	Yes (at operation)
L. C. HKH No. 106440		60	60	Sec. 60 1T	4T				260 6T	430	430	390	400		500		Yes (hysterectomy necessary)
E. W. HKH No. 97778			61	62	Sec. 62 1T	1T	107		342	784	666		804		792		Yes
S. L. HKH No. 119555			84	1T	Sec. 1T						262	326					No

*Normal fibrinogen levels: nonpregnant women 260; normal pregnancy at term 480; in pre-eclamptic women 510; in eclampsia 660.[19]
†Del. = vaginal delivery; Sec. = cesarean section; 1T = 500 c.c. blood transfusion.

after a prolonged operative procedure, the abdomen was finally closed successfully. Case L. C. required section and bled so profusely from the incision in the uterus and the bladder flap area that subtotal hysterectomy was necessary. There was then considerable difficulty in stopping bleeding from the cervical stump, despite numerous deep figure-of-eight sutures. Finally, after 2,000 c.c. of blood had been rapidly pumped into her, the clotting mechanism was restored and the operation was then quickly and easily completed. Case E. W. had a classical section four hours after admission and bled excessively during closure of the uterus, but blood transfusions and her own resources finally corrected this. Case S. L. required a section, but there was no definite evidence of a hemorrhagic tendency, and she received a 500 c.c. blood transfusion before, and another one during, this procedure. These two transfusions probably raised her fibrinogen level substantially above the initial 84 mg. per cent before the operation was commenced, and thus her probable hemorrhagic tendency had been corrected before operation.

Several interesting aspects of the "time element" in these cases can be seen in Table I. In the mild cases the length of time the abruption state continued without being terminated by delivery does not appear to have had any bearing on the severity of the disease in the patient. Such does not seem to be the case, however, in the moderately severe group. Case H. D., who had a fibrinogen level of 320 mg. per cent about six hours after the abruption commenced, must have had a much lower level at the time of delivery eight hours later if one transfusion and the passage of eight more hours brought her level up only to 250 mg. per cent. It would seem, therefore, that her degree of defibrination probably increased as she continued undelivered. She had chronic hypertension, and remained in moderate shock until three hours after delivery. Case M. C. went for ten hours following abruption before she was delivered (delivery occurred one hour following admission) and her fibrinogen is the lowest we have recorded. It was four hours after admission before we were finally able to match her blood properly and start a transfusion. In the meantime she, with her own resources, restored her fibrinogen to 200 mg. per cent. Case E. L. became very markedly defibrinated in the short space of two hours, and her stated time of onset of severe abdominal pain is correct because she happened to be in the hospital under surveillance for another condition at the time. In the next two hours, however, she restored her fibrinogen, half again, through her own resources, and the transfusion subsequently aided in correcting the hemorrhagic diathesis after one hour.

In from four to six hours following commencement of symptoms of abruption, all of the severe cases had become defibrinated to levels of 90 mg. per cent or lower, below which level, as our experience shows, there is usually sufficient disruption of the blood coagulation mechanism to result in clinical evidences of hemorrhagic diathesis. This excessive bleeding tendency was present in all of these severe cases except S. L., but she undoubtedly had her fibrinogen level raised by the preoperative blood transfusion so that, by the time the tissues were incised, she had thereby been rendered relatively safe for surgery.

It appears from Table I that the state of marked defibrination which occurs in the severe cases tends, in general, to continue until the uterus is emptied; it is also evident that it is wise to commence alleviation of this state by blood transfusion, even if only mild shock is present, before indicated operative measures to empty the uterus are commenced. In the moderately severe cases the degree of defibrination, like the proportion of the placenta separated, may vary from slight to great, and may tend to correct itself to some degree before delivery except in those cases in which the patient's condition is gradually worsening. There are no reliable clinical data which proportionately correlate the amount of placental separation with the degree of severity of constitutional manifestations of the disease.[11]

TABLE II. ANALYSIS OF CLINICAL STATE, TREATMENT, AND END RESULTS IN 10 CASES OF ABRUPTIO PLACENTAE

| CASES | DEGREE OF SHOCK | | | PRE-ECLAMPSIA OR ECLAMPSIA | TOTAL BLOOD GIVEN (C.C.) | PERCENTAGE OF NORMAL FIBRINOGEN* | HEMORRHAGIC DIATHESIS | DELIVERY | | HOURS AFTER ADM. | OLIGURIA | SURVIVAL | |
	MILD	MOD.	SEVERE					SECTION	VAGINAL			MOTHER	INFANT
Mild—													
M. S. HKH No. 112394	None			0	0	75	No		+	14	0	Yes	No (Twins)
E. B. HKH No. 98573	None			0	0	56	No		+	4½	+	Yes	Yes
Moderately Severe.—													
H. D. HKH No. 108744		+		0	500	57	No		+	8	+	Yes	No
M. C. HKH No. 117359		+		+	500	2	Yes		+	1	+	Yes	No
B. H. HKH No. 117626		+		+	500	27	No		+	4½	0	Yes	No
E. L. HKH No. 111278	None			0	500	9	Yes		+	10	+	Yes	No
Severe.—													
P. M. HKH No. 105006			+	0	4,600	20	Yes	+		7	+	Yes	No
L. C. HKH No. 106440			+	0	4,250	14	Yes	+		9	+	Yes	No
E. W. HKH No. 97778			+	0	1,100	14	Yes	+		4	0	Yes	No
S. L. HKH No. 119555			+	+	500	19	No	+		2	+	Yes	No

*A normal fibrinogen level of 440 mg. per cent was interpolated for the purpose of these calculations, since the average duration of pregnancy in this series was 33 weeks.[10]

Can we say, from our findings, that the longer the abruption state continues and the patient remains undelivered the more dangerous it is for her and her infant? The answer, in general, is "Yes." In the mild cases, if they remain mild, we do not, upon examination of the freshly delivered placenta, find evidence of extension of the separation beyond the initial hemorrhage and detachment. In the moderately severe cases, careful observation may frequently disclose clinical evidence of a primary episode, with subsequent episodes in addition. We also see placentas in which there is a depressed area, with its attached dark clot, and then an adjacent area of apparently fresher and more recent separation with its attached, brighter red clot, and thus it seems that there is frequently a continuous abruption process, advancing by stages, in these patients. These are the women who, clinically, seem to become progressively worse as they remain undelivered. In most of the severe cases there is total separation of the placenta and, since it is frequently found at section to be floating freely within a uterus full of serum and blood clot, most of which appears to be of the same relative age, one surmises that the placental separation rapidly became total in the initial abruption. In these cases there usually is a progressive worsening of the patient's condition, the apoplectic uterus cannot labor to empty itself, and section is frequently best resorted to as soon as possible and feasible, despite evidence that the baby is dead. The fact that the baby is believed to be dead, in a case such as this, should not be considered when the decision to perform section is being reached; section in a severe case may well be lifesaving for the mother and if one is dissuaded from it solely because the baby is already lost, the tragedy of a dead baby begetting a dead mother may be enacted.

General Consideration of Clinical Manifestations

In Table II we note that the mild cases fulfilled the requirements of their definition in that there were no shock, no necessity for blood transfusion, and no toxemia nor hemorrhagic diathesis. These patients likewise delivered vaginally and the only infant in our series that survived was born of one of them. Those with moderately severe cases evidenced from none to moderate shock, and each required one 500 c.c. blood transfusion. Two had toxemia and oliguria, three had hemorrhagic diatheses, and they all delivered stillborn infants vaginally. The four with severe cases had from moderate to severe shock, one had pre-eclampsia, another had oliguria for one day, and all four required section, by which completely separated placentas, blood clots, and dead infants were delivered. These four women required the transfusion of from one to nine 500 c.c. units of whole blood in order to correct their hemorrhagic diathesis and replace their lost blood.

Although the 10 cases presented cannot be used for statistical purposes, we can note that none of the mothers died, and this is believed to be ascribable to adequate and aggressive blood transfusion when and as needed and to rapid emptying of the uterus, when indicated, just as soon as was feasible and possible. A total of 11 infants were born, one of whom, despite a birth weight of 1,126 grams, survived and is well. Eight of the infants were stillborn, five of them premature while three were mature. The premature twins lived for only a few hours.

The mild cases required no particular treatment; delivery was spontaneous and thereby their problem was solved. Those with moderately severe abruption were almost always in good labor and proceeded fairly rapidly toward delivery. If such was not the case, and the bleeding persisted, we frequently performed artificial rupture of the membranes which invariably stimulated them into good labor. We do not believe it is wise to resort to Pitocin stimula-

tion of labor in those cases in which one might suspect the presence of any
degree of uterine apoplexy, namely, in those cases in which the uterus is not
relaxing well between contractions, nor do we use it in patients whose parity
is four or greater.

It is our belief that in most of the severe cases we are confronted with an
essentially different situation from that in the moderate or mild ones. In the
severe case the placenta is usually completely separated, the uterus is dis-
tended with blood and is not in labor, and the patient is in shock. She appears
to have bled into the uterus until it has expanded practically to its limits of
distensibility, and this is especially true in cases in which the cervix is long
and closed and there is little or no vaginal bleeding. It is believed unwise, in
a case such as this, to put one's finger forcibly through an undilated cervix
(when the patient is not and has not been in labor) and then to rupture the
membranes.[11] Experience has shown that too many such severe cases thus
treated have ended in fatal hemorrhage.[1, 2, 3, 4, 11, 12] It is believed that a case
such as this should rather have beginning blood replacement by transfusion
with whole citrated blood, followed rapidly by cesarean section which is per-
formed as soon as the operating room can be set up, and when the patient's con-
dition has ceased to grow worse, and the clotting power of the blood has been re-
stored. In our experience, any severely ill patient not in labor upon admission to
the hospital can seldom be made to go into effective labor, by whatever means,
and without labor she certainly cannot safely be made to deliver from below.

Comment

What has been the specific effect of the findings of our fibrinogen studies
upon our ideas of treatment? We believe that in many of the moderately
severe and most of the severe cases the abruption state, if permitted to con-
tinue overlong, will defibrinate the patient down to "hemorrhagic diathesis"
levels. Our studies have shown us that our moderately severe cases are not so
innocent in this regard as we formerly assumed, and that in them delivery
as soon as possible should be encouraged. Since these patients are practically
always in effective labor, section is rarely indicated. We believe that our
studies principally have shown us a rational and factual basis for treatment
practices which our trial-and-error experience had previously taught us,
namely, that if delivery is delayed too long in the severe case we may well lose
the patient because of uncontrollable hemorrhage.

It is believed that as long as the abruption state is permitted to exist it
will be constantly depleting the blood coagulation mechanism. The fact that
the abruption state appears to cause continuous utilization of the blood co-
agulation factors[5, 7] (of which fibrinogen and prothrombin[7, 8, 13] and accelera-
tor globulin[14] are important representatives) puts the major portion of the
load of continuous replacement of them on the patient's own resources. It
is conceivable that after several hours of this these resources may come to ex-
haustion and may not be able longer to meet the heavy demands of the situa-
tion. Since the amount of blood coagulation factors contained in whole, fresh,
citrated blood is sufficient to meet only a smaller portion of this demand, one
cannot fall back upon blood transfusion alone. The blood should rather be
used, we believe, as an early stopgap measure quickly to get the severely ill
patient into sufficiently good condition so that she can withstand the delivery
we are hastening to achieve for her before she goes on into an irretrievable
hemorrhagic diathesis state. This tragic state has been aptly described by
Kellogg,[5] when, in speaking of transfusing continuously and treating "con-
servatively" a severe case, he said: "This . . . has on occasion led to that
unpleasant situation in which more and more foreign blood has been given a

patient only to be washed out in what remains of the patient's own blood—her condition being such that one did not dare to stop the transfusions."

If one is confronted with a severe case, with a hard uterus, marked shock, and a long, closed cervix, and if the uterus is so damaged and overdistended that it can no longer evacuate the pregnancy by its own intrinsic contractile powers, it is up to the obstetrician to attack the dilemma through emptying the uterus by cesarean section. The obstetrician knows that a patient has to be in a relatively fair condition if she is going to be able to survive operation, so he should first pump blood into her in order to get her into the best condition possible, as rapidly as possible, and as soon as he has succeeded in this he should quickly perform the section.

Summary

1. Blood plasma fibrinogen determinations were performed on ten selected women having abruptio placentae, the specimens being taken before, during, and/or following delivery. These studies were made in order to evaluate the potentiality for development, in these cases, of a hemorrhagic diathesis state.

2. The two mild cases showed no defibrination. The four moderately severe cases showed varying degrees of defibrination, from mild to severe, the two with fibrinogen levels lower than 90 mg. per cent developing hemorrhagic diatheses. In all of the four severe cases there was marked defibrination and in three of them abnormally great tendencies to bleed were present.

3. Since the defibrination tends to continue until delivery, and to clear up following delivery, it must be caused by the abruption state, since delivery chiefly accomplishes abolition of this state. These studies also demonstrated that the defibrination state may continue or grow worse in some of the moderately severe cases as well as in the severe ones, and that it is therefore wise to hasten their delivery if need be.

4. The evidence that the hemorrhagic state occasionally occurring in cases of abruptio placentae is due principally to depletion of the fibrinogen is further substantiated by our findings. Dangerous degrees of defibrination can occur within one hour following the occurrence of abruption.

5. These patients were all successfully treated with blood transfusion, given as quickly as needed and in amounts sufficient to replace the blood loss and to help restore whatever disruption of the blood coagulation mechanism might have occurred.

6. The second part of their treatment was termination of the abruption state through delivery. The obstetrician must see that this is accomplished before there is depletion of the patient's blood coagulation mechanism to an irretrievably low degree. If the apoplectic, overdistended uterus in a severe case is unable to go into labor so that it can deliver itself of its pregnancy, a section should be performed. The section should be commenced, in the severe cases, just as soon as there is some bettering of the patient's condition by rapid blood transfusion.

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1512 ST. ANTOINE STREET

THE DURATION OF THE THIRD STAGE OF LABOR

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AS a sequel to a study of manual removal of the placenta, the duration of the third stage of labor as managed at the New York Lying-In Hospital was investigated in order to set a practical time for initiating the procedure in the absence of bleeding. The 4,066 deliveries occurring here in 1951 were the source of this information.

A search of the textbooks and the recent literature revealed relatively little data on the subject. The earliest reference quotes Dubois who, in 1836, stated that if the third stage were left completely to nature, it lasted 1 to 1½ hours. Clarke, in 1875, established the mean duration at 25 minutes. Cazeaux, in 1875, wrote that the placenta was expelled from the uterus within 15 to 25 minutes in most instances, but would lie in the vagina for longer periods of time. Robb, in 1899, found, too, that expulsion was accomplished for the most part in 10 to 30 minutes.

The more recent literature gives us information relative to the duration of the third stage, in most instances, when oxytocics were employed. Calkins, in 1933, stated that with careful management of the third stage, without oxytocics, the average duration was 4 minutes, and that approximately 88 per cent of the placentas were expressed within 10 minutes. Davis and Boynton, in 1942, in a study of the use of ergonovine in the third stage showed that the duration of the third stage was less than 10 minutes in 96 per cent, less than 3 minutes in 73 per cent, when ergonovine was given intravenously following delivery of the head or shoulder. Danforth, commenting on this paper, stated that the third stage averaged 7 minutes when Pituitrin was given intramuscularly following delivery of the infant, whereas previously it had averaged 15 to 20 minutes.

Method and Material

A certain variation in the duration of the third stage is to be expected with different methods of management. In general, the third stage of labor is managed in this clinic as follows: The placenta is permitted to separate spontaneously and to be extruded into the lower uterine segment or vagina, from whence it is delivered by gentle pressure on the fundus, using it as a piston, as well as by light traction on the cord. Separation is determined by fundal palpation, the uterus rising in the abdomen and assuming a globular shape, or more accurately by digital exploration of the vagina, cervix, and lower uterine segment to determine actual separation. The Credé maneuver is not performed, manual removal being preferred if the placenta fails to separate spontaneously. Some oxytocic is given following delivery of the infant, either ergonovine or Pitocin, intravenously or intramuscularly, as well as after the placenta.

Fig. 1 is a graph showing the duration of the third stage in all vaginal deliveries. The majority of placentas (62.6 per cent) were delivered within 5 minutes, with the greatest number being delivered in the second and third minutes. The longer third stage, in many instances, is a matter of choice, because, in the absence of immediate separation, the episiotomy is repaired.
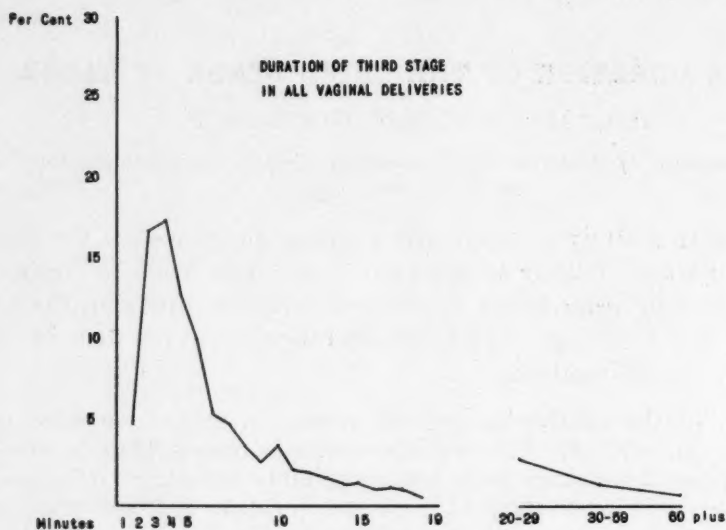
Fig. 1.

Table I illustrates in chart form the duration of the third stage in all vaginal deliveries. The placenta was delivered in less than 20 minutes in 95.1 per cent. In the next 10 minute period, only 2.9 per cent were delivered. Ninety-nine and three tenths per cent were delivered within 1 hour, and only 23 were delivered after an hour.

TABLE I. DURATION OF THIRD STAGE IN ALL VAGINAL DELIVERIES

MINUTES	NUMBER	PER CENT	CUMULATIVE PER CENT
0-19	3,868	95.1	95.1
20-29	119	2.9	98
30-59	51	1.3	99.3
60 plus	23	0.6	99.9
Unknown	5	0.1	100
Total	4,066	100	

In order to get a clearer picture of the duration of the third stage in spontaneous expulsion as compared to manual removal of the placenta, the remaining tables were prepared.

Table II shows that where the placenta was spontaneously expelled, it was accomplished within 30 minutes in 98.7 per cent, and only three were spontaneously expressed after one hour.

Table III shows that in manual removal of the placenta, 47.2 per cent were done within 20 minutes, and that 29.3 per cent were done after an hour. This mirrors the trend toward early prophylactic manual removal to shorten the third stage, especially in cases where the patient is already under general anesthesia. In previous years, early manual removal was done principally on the indication of excessive bleeding prior to completion of the third stage.

TABLE II. DURATION OF THIRD STAGE IN SPONTANEOUS EXPULSION OF PLACENTA

MINUTES	NUMBER	PER CENT	CUMULATIVE PER CENT
0-19	3,836	95.9	95.9
20-29	112	2.8	98.7
30-59	42	1.1	99.8
60 plus	3	0.1	99.9
Unknown	5	0.1	100
Total	3,998	100	

TABLE III. DURATION OF THIRD STAGE IN MANUAL REMOVAL OF THE PLACENTA

MINUTES	NUMBER	PER CENT	CUMULATIVE PER CENT
0-19	32	47.2	47.2
20-29	7	10.3	57.5
30-59	9	13.2	70.7
60 plus	20	29.3	100
Total	68	100	

Table IV shows the comparative incidence of the method of placental delivery relative to the duration of the third stage. In the cases where the third stage was completed within 19 minutes, 99 per cent were spontaneously expelled. As the duration of the third stage increases, the percentage of the placentas spontaneously expelled decreases, and the percentage manually removed increases, so that in the 23 cases where the third stage lasted over one hour, 87 per cent were manually removed.

TABLE IV. COMPARATIVE INCIDENCE OF METHODS OF PLACENTAL DELIVERY RELATIVE TO DURATION OF THE THIRD STAGE

MINUTES	SPONTANEOUS EXPULSION		MANUAL REMOVAL		TOTAL
	NO.	%	NO.	%	
0-19	3,836	99.2	32	0.8	3,868
20-29	112	94.1	7	5.9	119
30-59	42	82.4	9	17.6	51
60 plus	3	13	20	87.0	23
Unknown	5	100			5

Summary and Conclusions

The average duration of the third stage of labor in this series was 8.4 minutes; in spontaneous expression of the placenta, 3.9 minutes; in manual removal, 42.7 minutes.

The time-honored indication for manual removal of the placenta, retention for one hour in the absence of bleeding, is basically sound. Manual removal as early as 30 minutes after the birth of the child, however, will not increase the incidence of the procedure markedly, but should not be undertaken till all measures to combat hemorrhage and infection have been taken.

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ENDOMETRIOSIS IN THE OLDER AGE GROUP

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THE increasingly frequent recognition of endometriosis as a clinical entity has often been noted. It is now responsible for a large proportion of the gynecological laparotomies done in this country each year.

However, despite the frequency with which we deal with this condition, we are still largely in the dark as to its etiology and histogenesis. Several theories have been presented and ably championed, among which may be noted especially the retrograde menstruation theory of Sampson, the celomic metaplasia theory of Iwanoff and Meyer, and the concept of benign metastasis of endometrial tissue recently proposed by Javert.[1] Meigs[2] feels that the theory of celomic metaplasia is the correct one, and that the stimulus for the metaplasia is furnished by prolonged menstruation uninterrupted by pregnancy.

The evidence for and against these various theories has been discussed many times.[1-4] Suffice it to say that to date no one theory can be invoked to explain all cases of endometriosis.

Many investigators are tending to the belief that external endometriosis and internal endometriosis or adenomyosis may well be two different entities. The relationship, if any, of these two conditions is poorly understood.

Symptomatic endometriosis is usually a disease of menstrual life, and one gets the clinical impression that most of the more dramatic cases occur in comparatively young women. However, reports of several large series[2, 5-8] show that there is a rather high incidence of patients coming to surgery after the age of 35. The highest age incidence in most series is in the decade 31-40.

Our purpose in conducting this survey was to examine closely a group of older patients with endometriosis, namely, those 35 years of age and over. To our knowledge, the older age group as such has never been reviewed specifically in the literature.

We felt that this group of patients, having completed the major portion of their menstrual and childbearing careers, might give us a more accurate picture of the sort of menstrual and reproductive histories associated with endometriosis. For instance, it is difficult to assay the role of fertility in a girl who is subjected to pelvic surgery for endometriosis while still in her early twenties.

Since the childbearing career of most women is largely concluded by the age of 35, this age was arbitrarily selected as a dividing point.

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It was decided that it would be worth while at the same time to survey this group with regard to a number of other factors. Only by the patient accumulation of data can problems such as the etiology of endometriosis be solved.

It was thought that postmenopausal patients might be of particular significance with regard to possible etiological factors, inasmuch as endometriosis is said to be a disease of menstrual life dependent upon the estrogenic activity of the ovary. Accordingly the postmenopausal patients in our group, although included in the survey of the group as a whole, have also been taken up as a unit.

We have felt that a possible source of error in statistical reviews of endometriosis might be the fact that there are so often co-existent entities such as myomas, etc. Some of the symptoms and findings in these patients might be at least partially due to the associated pathology. Accordingly, those cases in which endometriosis has been relatively pure, so to speak—that is, without any associated pathology—have been studied as a group.

Material

Our material includes a consecutive, unselected series of all cases histologically diagnosed as endometriosis over the eleven-year period, 1940 through 1950. Both external and internal endometriosis have been included, and cases in which both conditions were present in the same patient were put in a separate class (combined external and internal).

A total of 696 cases of endometriosis were diagnosed microscopically in this eleven-year period. Of these, 433 were external, 206 were internal, and 37 were combined endometriosis. Of the 696 cases, 387, or 56 per cent, fell into the age group 35 and over. There were 200 cases of late external, 155 of late internal, and 32 of late combined endometriosis. In other words, 75 per cent of all cases of internal endometriosis were in the older age group, and 86 per cent of the combined group, whereas only 46 per cent of the patients with external endometriosis were in this category of 35 years of age and over.

All patients in this series were of the white race.

Due to variations in the adequacy of the histories reviewed, occasionally cases were excluded from the consideration of individual points which were being investigated.

Age Incidence

Of 197 patients with external endometriosis, 70, or 36 per cent, were aged 35 to 39 years; 67, or 34 per cent, were 40 to 44; 40, or 20 per cent, were 45 to 49; and 20, or 10 per cent, were aged 50 or over.

Of 155 patients with late internal endometriosis, 30, or 19 per cent, were aged 35 to 39; 41, or 26 per cent, were 40 to 44; 48, or 31 per cent, were 45 to 49; and 36, or 23 per cent, were aged 50 or over.

Of 31 patients with combined external and internal endometriosis, 10, or 32 per cent, were aged 35 to 39; 9, or 29 per cent, were 40 to 44; 5 or 16 per cent, were 45 to 49; and 7, or 23 per cent, were aged 50 or over.

These figures show the tendency of external endometriosis to occur in a younger age group than internal endometriosis or adenomyosis.

Incidence in Private Versus Ward Patients

In 199 patients with late external endometriosis, 173, or 87 per cent, were private patients, while 26, or 13 per cent, were ward cases.

Of 152 patients with late internal endometriosis, 121, or 80 per cent, were private patients, while 31, or 20 per cent, were ward cases.

Of 31 patients with late combined endometriosis, 26, or 84 per cent, were private patients, while 5, or 16 per cent, were ward cases.

The general incidence of service patients among the gynecological admissions to this hospital is roughly 20 to 25 per cent. Therefore, our figures here do not bear out the preponderance of private patients usually reported in series of endometriosis. However, due to the nature of the clientele of this hospital, the ward patients in general come from a somewhat higher socio-economic group than in most hospitals. But even so our figure is at variance with the usual finding.

Symptomatology

Of 200 patients with late external endometriosis, abnormal bleeding was noted by 121, or 60 per cent; 107, or 54 per cent, had dysmenorrhea; 102, or 51 per cent, had backache; 86, or 43 per cent, noted pain; 82, or 41 per cent, had a sensation of pelvic pressure; and 23, or 12 per cent, noted dyspareunia.

Of 155 patients with late internal endometriosis, abnormal bleeding was noted by 109, or 70 per cent; 58, or 37 per cent, had dysmenorrhea; 61, or 39 per cent, had backache; 54, or 35 per cent, noted pain; 68, or 44 per cent, had pelvic pressure; and 23, or 15 per cent, noted dyspareunia.

Of 32 patients with late combined endometriosis, abnormal bleeding was noted by 25, or 78 per cent; 18, or 57 per cent, had dysmenorrhea; 16, or 50 per cent, had backache; 13, or 41 per cent, noted pain; 12, or 38 per cent, had pelvic pressure; and 9, or 28 per cent, noted dyspareunia.

Many of these patients, of course, had multiple symptoms.

It is apparent that abnormal bleeding, dysmenorrhea, backache, and pain were the most common complaints. Dyspareunia was noted relatively seldom, perhaps because of the less active sex life of these older patients.

In general these results are in agreement with those previously reported. However, pelvic pressure was present in a large percentage of our patients, and we believe that its frequency has not hitherto been brought out. Frequently it is necessary to question the patient specifically upon this point, as the patient's sense of modesty may keep her from mentioning this complaint spontaneously. Many physicians, in taking histories, tend to gloss over such points as pelvic pressure for fear of embarrassing the patient. Pelvic pressure as we use it refers to a heavy sensation in the lower pelvis or vagina, somewhat as though the "womb was about to fall out." It is often noted in these cases particularly at the time of menstruation. The presence of this symptom has frequently been of diagnostic value to us, even in younger patients.

Previous Surgery

Of 197 patients with late external endometriosis, 70, or 35 per cent, had had some type of previous gynecological surgery, sometimes multiple. Appendectomies are not included in this survey. Thirty-eight, or 19 per cent, had had some type of vaginal surgery. This was chiefly dilatation and curettage, with a few cervical cauterizations and a few vaginal plastics. Eighteen, or 9 per cent, had had adnexal surgery, and 22, or 11 per cent, had had uterine surgery—suspensions, myomectomies, or cesarean sections.

Of 155 patients with late internal endometriosis, 75, or 48 per cent, had had previous gynecological surgery; 44, or 28 per cent, had had vaginal surgery; 12, or 8 per cent, had had adnexal surgery; and 28, or 19 per cent, had had uterine surgery.

Of 31 patients with late combined endometriosis, 12, or 40 per cent, had had previous gynecological surgery; 23 per cent had had vaginal surgery; 16 per cent had had adnexal surgery; and 7 per cent had had suspensions.

It must be recalled that these older patients had had a relatively long time to be exposed to pelvic surgery and pelvic surgeons. Still, this is a very high incidence of previous surgery. One is tempted to wonder if there may be an etiological connection, particularly in the case of internal endometriosis. The possibility that these operations were for an earlier manifestation of the same endometriosis which later brought the patient to the surgery covered in our series must be borne in mind. However, we believe that this possibility is precluded by the fact that the bulk of the previous operations were not done within five years of the surgery covered by our review.

Associated Pathology

Of 197 patients with late external endometriosis, there was no associated gynecological pathology in only 51, or 26 per cent. Myomas were co-existent in 114, or 58 per cent; relaxation of the vaginal outlet with or without cystocele and/or rectocele was present in 23, or 12 per cent. Endometrial hyperplasia was present in 19, or 10 per cent; retroversion of the uterus in 16, or 8 per cent; and salpingitis in 14, or 7 per cent. There were 3 cases of co-existent pregnancy, one of which was tubal; there were also found 5 cases of benign ovarian tumor and 2 cases of carcinoma of the fundus.

Of 155 patients with late internal endometriosis, there was no associated gynecological pathology in 29, or 19 per cent, of the cases. Myomas were present in 59, or 38 per cent; vaginal relaxation in 55, or 31 per cent; hyperplasia of the endometrium in 31, or 20 per cent; retroversion in 12, or 8 per cent; and salpingitis in 13, or 8 per cent. There were 4 cases of benign ovarian tumor. There were 5 cases of ovarian malignancy, and 1 carcinoma of the fundus.

In the combined group of 31 patients, there was no associated pathology in 8 patients, or 26 per cent; myomas in 15, or 49 per cent; vaginal relaxation and hyperplasia each in 3, or 10 per cent; retroversion in 7 per cent; and salpingitis in 16 per cent. Also associated with the 31 cases in the combined group were 1 case of carcinoma of the fundus and 1 case of carcinoma of the cervix.

By and large these figures are in essential agreement with published results. However, it is worth noting that Javert[1] states that carcinoma of the fundus occurs with greater frequency in patients with endometriosis. In our entire series of 383 patients in the older age group in whom information was available on this point, there were 4 cases of carcinoma of the fundus, an incidence of just over 1 per cent.

Fertility

This is a most important topic for investigation, because it has been accorded so much prominence in recent speculation regarding the etiology of endometriosis.

In our survey one year of marriage without pregnancy has been arbitrarily selected as the criterion for "sterility." On this basis, patients who have not conceived but who have been married for less than 12 months have been excluded from the statistics. The interplay of such factors as remarriage, voluntary contraception, wartime separations, and faulty memories probably operate to make many surveys subject to some error. For this reason we have not attempted to determine a pregnancy rate in terms of patient-months of exposure. Our survey is simply in terms of the number of pregnancies per patient.

Table I summarizes the over-all results. Twenty-seven per cent of married patients with external endometriosis were sterile, and 12 per cent of the group were single. So nearly 40 per cent of all the patients with external endometriosis had never been pregnant. In all, 273 pregnancies had occurred in 162 married women in this group on whom data were available, an average of 1.7 pregnancies per married patient. Forty-two abortions had occurred in the 119 patients who had been able to conceive, so that 18 per cent of all pregnancies had terminated in abortions.

TABLE I. ENDOMETRIOSIS AND PREGNANCY

TYPE OF ENDO- METRIOSIS	NO PREG- NANCIES (MAR- RIED)	ONE PREG- NANCY	TWO PREG- NANCIES	THREE PREG- NANCIES	OVER THREE PREG- NANCIES	PA- TIENT SINGLE	TOTALS
External.—	43 27%	35 2 abortions	48 9 abortions	15 7 abortions	21 patients 97 pregnancies 24 abortions	23 10%	273 pregnancies in 162 married patients. 1.7 average
Internal.—	7 5%	18 3 abortions	34 8 abortions	26 12 abortions	61 patients 352 pregnancies 83 abortions	8 5%	516 pregnancies in 146 married patients. 3.5 average
External and Internal.—	7 26%	3 1 abortion	7 1 abortion	3	7 patients 31 pregnancies 6 abortions	3 10%	57 pregnancies in 27 married patients. 2.1 average

In the patients with internal endometriosis or adenomyosis, the situation was very different. Only 5 per cent of the married patients were sterile, and only 5 per cent of the group were single. Not quite 10 per cent of the entire group had never been pregnant. There were 516 pregnancies in 146 married patients, an average of 3.5 pregnancies per married patient. There were 106 abortions in 139 patients who were able to conceive, and over 20 per cent of all pregnancies had terminated in abortions.

In the group of patients with combined external and internal endometriosis, the figures show an average of 2.1 pregnancies per married patient, and an incidence of 25 per cent sterility among 27 married patients. Thirty-three per cent were either sterile or single and had never conceived; 17 per cent of all pregnancies terminated in abortions.

Some contrasting tendencies are apparent in these figures: 12 per cent of patients with external and 5 per cent of those with internal endometriosis were single. According to U. S. Census statistics,[11] 9 per cent of women in the age group 35 to 44 years are single.

Of the married patients in our series, 27 per cent of those with external endometriosis were sterile, as opposed to only 5 per cent of those with adenomyosis. According to U. S. Census figures,[11] about 16 per cent of all married women between the ages of 45 and 54 years (i.e., of completed fertility) are childless.

Furthermore, the average number of pregnancies per married patient with external endometriosis is only 1.7, and the average number of children is only 1.4. In married patients with internal endometriosis, the average number of

pregnancies is 3.5, and the average number of children is 2.7 plus. Census figures[11] show that, surveying all children ever born to married women aged 45 to 54, the average figure is about 3.0 children per married woman.

There can be no question but that, in patients with external endometriosis in the older age group in this series, the percentage of spinsterhood, sterility, and low fertility is higher than is the case for the average woman. Since these patients have had ample time to demonstrate their fertility prior to the onset of endometriosis, we believe that we have here definite evidence that sterility and low fertility precede external endometriosis in a statistically significant manner. A disease becoming clinically manifest around the age of 35 or over could hardly cause that same patient to be sterile during her twenties.

Also of importance, and hitherto not stressed, is the high incidence of spontaneous abortion in patients with endometriosis. The incidence of spontaneous abortion in the population at large averages in the neighborhood of 10 per cent, varying from 9 per cent to 13 per cent in several large series. In our external endometriosis group of 119 fertile patients, there were 42 abortions by 27 patients. This means that 18 per cent of all pregnancies ended in abortion, and that 23 per cent of the fertile patients had at least one abortion. In 139 fertile patients with adenomyosis, there were 106 abortions by 57 women—that is, 21 per cent of all pregnancies ended in abortions, and 41 per cent of the fertile patients aborted at least once. These figures are large enough to be of definite significance.

U. S. vital statistics for 1948[12] show that, at the birth of over one million first children, the mother was aged 15 to 19 in 26 per cent of cases and 20 to 24 in 42 per cent—a total of 66 per cent prior to the age of 25 years. For our series of external endometriosis, the corresponding figures were 8 per cent and 45 per cent, a total of 53 per cent prior to age 25. In patients with adenomyosis, the figures were 28 per cent and 42 per cent, a total of 70 per cent prior to the age of 25. Our patients with external endometriosis had their first pregnancies at an average age of 24.4 years; with internal endometriosis it was 22.6 years. The age at the time of the last pregnancy was 29.3 years with external and 30.4 with internal endometriosis.

Cases With No Associated Pathology

Prior to this study we felt that a possible source of error in the consideration en masse of all patients with endometriosis might be the frequent presence of the many conditions which coexist with endometriosis. We found that an attempt to select those cases in which endometriosis was the primary condition was difficult and often impossible, and would therefore often be misleading. However, cases in which endometriosis was the only pathological finding (excluding also cases with retroversion or vaginal relaxation) should offer an opportunity to study the disease in an unquestionably pure form. There were 90 patients available in this category, 52 with external, 30 with internal, and 8 with combined endometriosis.

The average age of these patients was just over 41 years in external and just under 43 in internal; in combined endometriosis it was just under 42 years.

There were 46 private and only 6 ward patients with external endometriosis; 29 private and only one ward patient with internal; and 7 private and one ward patient with combined endometriosis. So the preponderance of private patients in this disease is accentuated in this group.

Of the 52 patients with external endometriosis in this group, 60 per cent noted abnormal bleeding and 60 per cent had dysmenorrhea; 54 per cent noted pelvic pain; 48 per cent had backache; 33 per cent noted pelvic pressure; and 17 per cent suffered from dyspareunia.

Of 30 patients in the internal group, 77 per cent noted abnormal bleeding; 43 per cent had dysmenorrhea; 47 per cent noted pelvic pain; 40 per cent had backache and 40 per cent had pelvic pressure; and 13 per cent had dyspareunia.

Of 8 patients in the combined group, 100 per cent noted abnormal bleeding; 50 per cent had pain and 50 per cent had backache; 75 per cent noted dysmenorrhea; and 25 per cent had pelvic pressure. None complained of dyspareunia.

In general, it may be said that the symptomatology displayed here parallels that of the entire group of cases. Once again the frequency of pelvic pressure as a symptom of endometriosis is demonstrated.

Previous gynecological surgery had been undergone by 42 per cent of patients with external, and 53 per cent of those with internal unassociated endometriosis; 21 per cent of the external and 40 per cent of the internal group had had vaginal surgery; 31 per cent of the external and 47 per cent of the internal group had had abdominal pelvic surgery (some patients had had multiple surgery).

Table II summarizes the position of fertility in this group of patients.

TABLE II.   "UNASSOCIATED" ENDOMETRIOSIS AND PREGNANCY

TYPE OF ENDO-METRIOSIS	AVERAGE AGE AT FIRST PREG-NANCY (YEARS)	MARRIED	NO PREG-NANCIES (MAR-RIED)	SINGLE	TOTAL NUMBER OF PREG-NANCIES	TOTAL NUMBER OF ABORTIONS	AVERAGE NUMBER PREG-NANCIES PER MARRIED PATIENT
External.— 52 cases	25.2	46	10	6	85	15 in 13 patients	1.8
Internal.— 30 cases	22.5	27	1	1	64	11 in 8 patients	2.4

Of married patients with external endometriosis, 22 per cent proved to be sterile, whereas only 4 per cent of the adenomyosis group were sterile. This contrast is even more striking than in the over-all group. Six more patients in the external group were single, a total of 31 per cent in this category who had never been pregnant. Only 1 patient in the group with adenomyosis was single, giving a total of only 7 per cent of these patients who had never been pregnant.

The external group had an average of 1.8 pregnancies, with an abortion rate of 18 per cent; 36 per cent of the fertile patients had aborted at least once. In the internal group the pregnancy rate was 2.4 per patient, with an abortion rate of 17 per cent; 31 per cent of the fertile patients had had at least one abortion.

Once again the first pregnancy tended to occur at a later age in the external group; only 36 per cent had been pregnant prior to the age of 25, as opposed to 71 per cent of the internal group.

The data relating to fertility in the combined group here were available in so few patients as to be considered not reliable. Hence they have been omitted from consideration.

Postmenopausal Patients

The patients with endometriosis who are postmenopausal are of particular interest in a survey of the older age group. We define "postmenopausal" as one year past the cessation of menses. According to the generally accepted

view, these are patients in whom the endometriosis represents the burned-out residuum of a process which was present during the patient's menstrual life. According to Siegler,[7] "After the menopause, endometriosis becomes only an asymptomatic relic." Our series is small, but we believe that it brings up some interesting points.

Our postmenopausal series includes 32 patients. In three of these the menopause was artificial. In two instances the patient had had a subtotal hysterectomy, two to four years prior to her surgery for endometriosis; in the other, menopause had been brought about by x-ray therapy 18 years previously.

The average age in 9 patients with external endometriosis was 57.0 years; three were 60 or over. The average age of menopause for these patients was 50.0. In 19 patients with adenomyosis the average age was 55.1, and the average age at menopause was 47.9. In 4 patients with combined endometriosis the figures were 55.8 and 50.0. Only those patients with natural menopauses have been considered in this calculation.

This group includes 27 private and 5 ward patients.

Our tabulation of symptomatology is more or less in accord with those previously given. However, fully 50 per cent of our patients noticed postmenopausal bleeding. If these cases represent merely an old burned-out condition, why should vaginal bleeding be so prominent? It appeared as late as 18 years after the cessation of normal periods.

Our survey of associated pathology is more or less in accord with the results for the whole group. In 7 of these postmenopausal cases there was no associated pathology. Three had fundal carcinomas, and one patient had a granulosa-cell tumor of the ovary, while there were four cases of benign ovarian tumors.

The incidence of previous surgery and fertility in these patients was not unlike that in the entire group of patients.

In the postmenopausal group there were 8 patients who were 60 years of age or over. The oldest patient, who had a large symptomatic endometrial cyst, was 75 years old.

Of especial interest are the 16 patients who had postmenopausal bleeding (50 per cent of the postmenopausal group). In 4 of these there was no associated pathology; in two more the patient had vaginal relaxation and mild pelvic inflammatory disease, respectively. In six other cases there were associated myomas, which rarely should produce this type of bleeding in themselves. In the other 4 cases there were the malignancies noted above. There seemed to be no significant relationship of postmenopausal bleeding to parity or to the number of years the patient was beyond the menopause.

Why postmenopausal bleeding should occur in a benign lesion such as endometriosis is difficult to understand. It is possible that, if high estrogenic activity is concerned in the etiology of endometriosis, it is likewise concerned with the bleeding phenomenon.

At any rate, we believe that this series of cases with postmenopausal bleeding is suggestive, and that further investigation of endometriosis after the menopause is warranted.

Summary

In order to get a better over-all understanding of the gynecological picture in patients who are destined to have endometriosis, a series of patients aged 35 years or over, with pathologically proved endometriosis was reviewed. External endometriosis, internal endometriosis or adenomyosis, and cases of both external and internal endometriosis were reviewed separately.

Abnormal bleeding, dysmenorrhea, backache, pelvic pressure, and pain were the most common symptoms in all types of endometriosis. Abnormal bleeding was found in about two-thirds of the cases. The importance of pelvic pressure as a symptom has not been sufficiently emphasized.

Forty per cent of our patients with external and over 50 per cent of those with internal endometriosis had undergone previous gynecological surgery.

In only one-fifth of our cases was there no coexistent clinical or pathological gynecological condition. Myomas were present in 58 per cent of the cases of external and 38 per cent of cases of internal endometriosis. Vaginal relaxation and endometrial hyperplasia were found more often in conjunction with adenomyosis. Retroversion was present in only 8 per cent of our cases.

Spinsterhood, sterility, and low fertility were definitely more common in external endometriosis than in the population at large. This was not true of internal endometriosis. This is felt to be of etiological significance. Pregnancy begins at a later age than normal in patients destined to have endometriosis. The rate of spontaneous abortion was double the normal incidence in both types of endometriosis.

In patients with pure endometriosis not associated with other conditions, all the above results concerning pregnancy were borne out and emphasized. The preponderance of private over ward patients was especially high in this group. Symptomatology, previous surgery, and associated pathology were roughly parallel in their incidence to that found for the entire group of patients.

The 32 postmenopausal patients in this series showed a 50 per cent incidence of postmenopausal bleeding. It is felt that this may throw some doubt on former beliefs that endometriosis after the menopause is only a relic. Further study of this group of patients is indicated.

The most striking contrast between external and internal endometriosis lies in the different roles of pregnancy and fertility in the natural history of these conditions. The group of patients with combined external and internal endometriosis showed no characteristics which would warrant their being considered as a separate class.

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VIRAL DISEASES IN PREGNANCY AND THEIR EFFECT UPON THE EMBRYO AND FETUS*

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SINCE the publication by Gregg[1] and Swan and associates[2] of the tragic results of maternal rubella in early pregnancy upon the offspring, a marked interest has been shown concerning the relationship of maternal illness to fetal anomalies. While rubella is generally recognized as a potent source of embryonic damage, the effects of other virus diseases upon the embryo are not well documented. This was brought to our attention forcibly when we encountered three instances of viral disease in pregnancy in a single month. Two of these presented no particular problem and will be discussed later. However, the third, a case of ordinary measles in the second month of pregnancy, caused us great concern because the patient had been advised by another physician to have a therapeutic abortion. In view of the dire effects upon infants born to mothers suffering from rubella in early pregnancy, and the widely recognized indication for therapeutic abortion in such instances, we were faced with the problem of whether or not our patient should be allowed to proceed to term. We found the medical literature meager on this subject and therefore initiated this investigation in an attempt at clarification.

The dangers of congenital anomalies of the fetus subsequent to maternal rubella in early pregnancy have been widely reported in the past ten years. In a recent symposium on congenital anomalies, Miller[3] surveyed a total population of 32,000 individuals and found 331 cases of maternal rubella, of which 110 occurred in the first trimester of pregnancy. He reported that the risk of fetal damage from maternal rubella occurring in the first trimester of pregnancy is about 40 per cent. Swan and co-workers,[6] in reporting on their work done in Australia, found 102 defects in 120 cases of maternal rubella—an incidence of 80 per cent. Gregg stated that 100 per cent of the infants born of mothers with rubella in the first trimester would have congenital cataracts. In Australia, major epidemics of this disease occurred in 1914, 1923, and 1937. Therefore, in the years between 1923 and 1937, there was little opportunity for contraction of the disease in epidemic proportions. In the years between 1937 and 1942, the vast majority of young adults and women of childbearing age—not having been exposed previously—were susceptible. Swan was unable to determine the total number of cases of maternal rubella in which the infants were unscathed. Later reports from Australia and elsewhere indicated that the highest incidence of fetal damage occurred when the mother contracted the disease in the first month of pregnancy. The percentage of anomalies decreased as the illness occurred in the succeeding months of gestation; after the fourth month of pregnancy, it was no longer a menace.

Since the original work done by Gregg, there have been a great many reports[3-11] that congenital cataract frequently resulted from maternal rubella. It has also been shown that there is a distinct rubella syndrome which includes cataract, congenital cardiac disease, deafness, and central nervous system damage. However, there is a paucity of reports concerning the effect of other maternal virus diseases upon the offspring. A review of the available world literature reveals that the risk of congenital anomaly is distinctly less than that which occurs with rubella. Some standard textbooks[12, 13, 14] which now include the effects of rubella during pregnancy disregard the occurrence of anomalies after other virus diseases, but do mention their role in the etiology of abortion. A high fetal mortality rate as a result of maternal measles and smallpox was reported by Lynch[15] in 1932.

The first extensive series of fetal anomalies following maternal rubella, reported by Swan and associates from Australia in 1943, included a few instances of anomalies following other maternal viral diseases. These authors stated that in the majority of cases, a severe virus infection killed the fetus whereas rubella maimed the surviving fetus. Subsequently Swan and his co-workers[6] noted 13 abnormalities and one abortion which occurred in 33 cases of maternal viral disease other than rubella. These occurred chiefly after attacks of mumps and influenza.

Dogramaci and Green[16] reported that of 1,387 women admitted to the contagious unit of Boston City Hospital in 1947, 17 were pregnant and only 6 were in the first half of pregnancy. Two of the 6 were afflicted with virus diseases and there were no major defects noted in the offspring. In 434 cases of congenital heart disease, a history of maternal virus infection occurring in the first trimester was found in only 9 instances. These included 6 cases of rubella, 1 of poliomyelitis, and 2 of "virus grippe." In addition, there were 8 cases of acute bacterial infection and 2 of acute rheumatic fever in the first trimester.

From Sweden, Wallgren[17] and Grönvall and Selander[18] reported in 1948 that mumps appeared to be the most frequent source of danger for the fetus in that country. These authors believe that 5 per cent of congenital anomalies are due to maternal viral infection in early pregnancy.

In a survey of 297 women afflicted with measles, mumps, or varicella, Fox and associates[19] found only 33 cases during pregnancy. Of those cases, only 8 were in the first trimester and in none was there a congenital anomaly in the offspring. In 1950, Schwartz[20] reported on mumps in pregnancy. Seven of his patients were in the first trimester and in none was any anomaly of the infant noted. One patient aborted in the fourth month of pregnancy following an attack of mumps.

In reports by Stevenson and co-workers,[21, 22] only 1 per cent of mothers with abnormal children gave a history of any type of febrile illness occurring in the first trimester. No specific mention was made of virus infections. About 10 per cent of the mothers had some form of chronic illness. Thirteen per cent of the patients gave a history of threatened abortion. These authors speculated on the possible role of anoxia as a teratogenic agent since 39.4 per cent of the mothers had a hemoglobin level below 75 per cent. They found a rate of 1.7 per cent malformed infants among all the births over a 12 year period. They also noted that 16 per cent of the total stillbirths and 13 per cent of the neonatal deaths were of malformed infants.

In 1951, Hartman and Kennedy[23] of the Mayo Clinic reported on the effect of first trimester illness on the fetus. They found no significant difference between the incidence of anomalies, premature births, or stillbirths in those mothers who had had acute illnesses in the first three months and in those who did not. Of 5 mothers with virus disease in the first trimester, no fetal anomalies occurred.

In a review of congenital defects, Bass[10] stated the following: (1) cataracts result from damage in the sixth week of gestation; (2) Mongolism in the seventh to ninth week; (3) deafness in the ninth week; (4) cardiac anomalies from the fifth to the tenth week; (5) deformed teeth in the sixth to the ninth week; (6) cleft palate in the eighth to the eleventh week.

Schick[24] has injected a new theory on the subject of maternal illness and its relationship to fetal abnormalities. He postulated that fetal infection by rubella or other viruses might occur in immune mothers. He cited the analogy of smallpox infection in fetuses of immune mothers. Schick quoted Warkany's case of an infant born with the rubella syndrome anomalies whose mother was not ill but who cared for her two other children with rubella when she was in the second month of pregnancy. His theory seems plausible and he warns that pregnant women should avoid contact with patients having rubella or possibly other virus diseases even when the women themselves are immune. Hagströmer[25] also reported similar instances in which two mothers, both of whom were immune and had had no disease during pregnancy, were exposed in the second month of pregnancy to ordinary measles. Both infants were born with cleft palates.

Material and Methods

We have elected to study our problem by the use of epidemiologic and statistical methods. We have reviewed records of all children born with congenital anomalies who were delivered at Michael Reese Hospital between Jan. 1, 1945, and Jan. 1, 1950, and those who were treated at Sarah Morris Hospital for Children during the same five-year period. We have selected only the serious anomalies such as congenital heart disease, Mongolism, cataract, hydrocephalus, pyloric stenosis, cleft palate, atresia of the bowel, and spina bifida. We have excluded such conditions as nevi and supernumerary digits. Our review included 376 records. We attempted to follow all cases by means of a questionnaire to the mother and by contacting the individual attending physicians whenever possible. The questionnaire included inquiries as to any illness, bleeding, or body rash at any time during the particular pregnancy, with specific reference to maternal mumps, measles, varicella, rubella, or scarlet fever. Questions concerning the child's health and the occurrence of any other anomalies in the family were also asked. Of the 376 questionnaires which were mailed, we received 196 replies. We were able to trace 77 more by other means. Our total series of cases included 273 congenital abnormalities; the types and number of specific anomalies appear in Table I.

Results of Michael Reese Hospital Series

When we initiated our review of the records of the congenital anomalies at Michael Reese Hospital, we were interested chiefly in the role of virus diseases in the etiology of the anomalies. However, it soon became apparent that virus diseases were not the preponderant contributory factors. Among our 273 cases of anomalies which were followed adequately, we found 90 instances in which there were possible etiological factors (Table I). There were a total of 33 cases of bleeding during pregnancy with 25 occurring during the first trimester. The 25 threatened abortions which resulted in abnormal children coincide remarkably with the series presented by Burge[32] in 1951.

There were 15 cases of acute illness during pregnancy, i.e., illness serious enough to merit reporting (Table II). Only 7 of these occurred in the first trimester. Eighteen mothers suffered from some form of chronic but not necessarily life-threatening illness (Table III). Eight of these women had had normal children previously during such chronic illness. There were also

TABLE I. INCIDENCE OF POSSIBLE PRENATAL FACTORS IN CONGENITAL ANOMALIES
(MICHAEL REESE HOSPITAL)

ANOMALY	TOTAL CASES	PRENATAL FACTOR
Cardiac	42	13
Cleft palate	26	9
Mongolism	22	14
Skeletal	34	6
Calcaneovalgus	15	
Equinovarus	6	
Absence of bones or extremities	4	
Dislocated hip	4	
Syndactyly	3	
Achondroplasia	2	
Genitourinary	7	3
Hypospadias	4	
Absent kidneys	1	
Congenital urethral stricture	1	
Persistent urogenital sinus	1	
Eye	11	5
Cataracts	9	
Corneal opacities	2	
Central Nervous System	34	14
Meningocele	14	
Hydrocephalus	8	
Anencephaly	5	
Microcephaly	4	
Cerebral agenesis	3	
Gastrointestinal	76	20
Congenital pyloric stenosis	61	
Intestinal atresia	6	
Imperforate anus	4	
Atresia of bile ducts	3	
Omphalocele	2	
Miscellaneous	21	6
Tracheoesophageal fistulas	7	
Ectodermal defect	6	
Branchial cyst	3	
Congenital cysts of lung	2	
Absent diaphragm	2	
Pseudohermaphrodite	1	
Total	273	90

9 other cases in which anomalies had occurred in siblings or other members
of the family, and the mother had had no illness during pregnancy (Table IV).

There were 23 cases of miscellaneous prenatal factors which were questionable as causes of congenital anomalies. Among these, there were 8 cases of Mongolism in which the mothers were from 36 to 43 years of age. In one, the father was 68 and the mother 43 at the time of the birth of their Mongoloid child. It is generally recognized that Mongoloid infants occur more frequently in mothers of older age groups.

Our personal series of private cases of maternal virus disease includes 2 cases of mumps, 1 case of measles, 1 case of varicella, 1 case of infectious mononucleosis, and 1 case of virus pneumonia. One case of mumps occurred at the eighth week of pregnancy and was followed by a spontaneous abortion. The other case of mumps occurred in the seventh month and a normal infant was delivered at term. Our case of measles occurred at the eighth week of pregnancy, the pregnancy went to term, and the patient delivered a normal child.

TABLE II. ACUTE ILLNESS (VIRAL DISEASE)

CASE NO.	AGE	PARITY	ILLNESS	CONGENITAL ANOMALY
First Trimester.—				
G85	24	i	Influenza with high fever at second month	Pyloric stenosis
C21	–	i	German measles at second month	Congenital cardiac disease
C34	24	i	Measles at first month (Pre-eclampsia)	Congenital cardiac disease
CN2	30	iv	Influenza at third month (Hypertension and obesity)	Pseudohermaphrodite and cerebral agenesis
CN27	25	ii	Severe "cold" in second month	Microcephaly and hydrocephalus
CN46	27	i	Virus pneumonia with high fever at fourth week	Anencephalus
M1	22	i	Influenza or "virus X" at third month	Mongolism
Second Trimester.—				
G27	–	i	Influenza at fifth month	Pyloric stenosis
C4	28	ii	Mumps at sixth month	Congenital cardiac disease
CN44	33	ii	Pertussis at fourth month	Cerebral agenesis
M17	28	i	Influenza at sixth month	Mongolism
Mi1	26	ii	Influenza at sixth month	Congenital ectodermal defect
Mi6	–	ii	Influenza at fourth month	Congenital cyst of the lung
Third Trimester.—				
G87	–	–	Influenza at seventh month	Pyloric stenosis

Our case of severe varicella occurred at the sixteenth week of pregnancy; 6 weeks later, the patient had a spontaneous miscarriage. The fetus showed no demonstrable abnormalities. This same patient subsequently had two premature deliveries resulting in living children so that it is possible that the varicella had no effect on the pregnancy. The patient with infectious mononucleosis at the second month had a normal term infant.

Our final case of virus disease was extremely interesting. This primigravida suffered an attack of virus pneumonia with a very high fever at the time of her first missed period. She subsequently delivered a 5½ month fetus which had spina bifida and anencephalus. Therefore, of our series of 6 cases of virus disease in pregnancy, 3 resulted in normal infants; 1 resulted in an early spontaneous abortion; 1 patient delivered a normally developed fetus at 22 weeks; 1 delivered a grossly malformed fetus at 22 weeks.

We had an interesting case recently which may be fittingly reported at this time, although it was not one of maternal virus infection. The patient was a 24-year-old white woman whose last menstrual period started on Dec. 15, 1950. She was seen by her physician on Feb. 7, 1951, because of an acute onset of chills, headache, diffuse arthralgia, and a fever of 103° F. She was treated with penicillin and Chloromycetin at home and in the hospital. Her temperature continued to spike daily until the tenth day of treatment; thereafter she ran a low-grade fever for several days. Blood culture on February 15 revealed *Eberthella typhosa*. Agglutination tests and stool cultures were positive for typhoid fever. She made an uneventful recovery thereafter and the remainder of her pregnancy was normal. On Oct. 4, 1951, she delivered a full-term male infant who seemed normal at birth. At the present time, a diagnosis of acyanotic congenital heart disease of undetermined type has been made on the infant by the attending pediatrician. This case represents the probable etiological significance of the acute maternal illness with high fever at the time of fetal development.

TABLE III. CHRONIC ILLNESS (NONVIRAL)

CASE NO.	AGE	PARITY	ILLNESS	CONGENITAL ANOMALY
G6	–	–	Petit mal	Pyloric stenosis
G10	27	ii	Asthma and food allergy	Pyloric stenosis
G49	40	ii	Hay fever and chronic arthritis	Pyloric stenosis
C18	31	iv	Hay fever (1 sibling had congenital cardiac disease)	Congenital cardiac disease
CN34	–	i	Asthma and spastic colitis ("4 day labor")	Microcephaly and "spastic"
Mi3	21	i	Treated syphilis during pregnancy (Penicillin)	Tracheoesophageal fistula, congenital cardiac disease and cleft palate
E2	31	ii	Treated syphilis and hypertension (Heavy metals)	Congenital cataract
CP17	26	ii	Treated syphilis 1 month before conception (Heavy metals)	Cleft palate
CN20	–	i	Treated syphilis during pregnancy; diabetes (Heavy metals)	Hydrocephalus
CN39	18	i	Treated syphilis and hypertension (Heavy metals)	Cystic aplasia of brain
C31	25	i	Treated syphilis during pregnancy (Heavy metals) and rheumatic heart disease	Congenital cardiac disease
G97	–	–	Chronic pyelonephritis	Pyloric stenosis
S42	28	i	Rheumatoid arthritis, rheumatic heart disease and hyperemesis at sixth week	Calcaneovalgus
S26	28	iii	Rheumatoid arthritis and bronchiectasis	Congenital dislocated hip
CP28	–	iv	Rheumatic heart disease and hyperemesis	Cleft palate
GU2	33	ii	Mild hypothyroidism	Hypospadias
M22	39	i	Hypothyroidism	Mongolism
CP18	–	i	Arrested pulmonary tuberculosis receiving pneumothorax	Cleft palate

TABLE IV. HEREDITARY FACTOR

CASE NO.	AGE	PARITY	FAMILY HISTORY	CONGENITAL ANOMALY
G1	35	viii	2 siblings with imperforate anus	Imperforate anus
CN3	35	iii	2 normal children prewar; since husband's return from service had 1 spontaneous abortion	Spina bifida and hydrocephalus
CN3	36	iv		Spina bifida and hydrocephalus
CP7	–	iii	Sibling has cleft palate	Cleft palate
CP10	–	–	Paternal uncle has cleft palate	Cleft palate
CP12	25	–	Paternal uncle has cleft palate	Cleft palate
E7	36	iv	Mother and 3 close relatives had congenital cataracts	Congenital cataracts
E9	–	i	Mother and 3 maternal siblings had congenital cataracts	Congenital cataracts
C18	31	iv	Sibling died of congenital cardiac disease	Congenital cardiac disease

Results of Survey of Cases in Literature

We have tabulated the reported cases in the literature and included our own cases in an attempt to discover the expected incidence of anomalies following maternal virus diseases. Unfortunately, we were unable to determine accurately the total number of cases of first trimester illness following which

normal infants were born. A rough survey revealed a total of 340 cases of virus diseases in pregnancy; of these, no less than 154 occurred in the first trimester. There were 113 normal infants born of this first-trimester group; there were 11 abortions and 30 abnormal fetuses (21 per cent). There were also 18 anomalies and 21 abortions in the group of 186 cases of virus diseases occurring after the first trimester, or at an unknown time during pregnancy. It was impossible to divide this latter group of 186 cases into the specific trimester because of lack of information in the published reports. As a result, the latter figure of 18 anomalies out of 186 pregnancies cannot be considered accurate.

Of the specific diseases, we have tabulated 103 cases of mumps in pregnancy. There were 17 infants with various major anomalies in this group. Nine of these occurred after mumps in the first trimester. There were also 4 abortions (Table V).

There were 63 cases of measles in pregnancy resulting in 10 congenital anomalies and 4 abortions. Of the 10 anomalies, 7 occurred as a result of illness in the first trimester (Table V).

We have found only 26 cases of varicella of which 3 resulted in congenital anomalies. There was one incidental stillbirth and one abortion at 22 weeks—the latter of a normal fetus, but the abortion occurred 6 weeks after a severe case of varicella (Table V).

There were also other diseases in pregnancy with their resultant anomalies which are recorded in Table V.

TABLE V. COLLECTED CASES OF MATERNAL VIRUS DISEASE IN PREGNANCY AND INCIDENCE OF
ANOMALIES

DISEASE	TOTAL CASES	ANOMALIES	PER CENT	ABORTIONS	PER CENT
Mumps	103	17	16.5	4	3.9
Measles	63	10	15.9	4	6.4
Varicella	26	3	11.5	0	–
Poliomyelitis	101	6	5.9	19	18.8
Infectious mononucleosis	8	3	–	1	–
Infectious hepatitis	31	1	3.2	4	12.9
Influenza	5	5	–	–	–
Herpes zoster	2	2	–	–	–
Virus pneumonia	1	1	–	–	–
Total	340	48	14.1*	32	9.4

*Excluding abortions.

The total incidence of anomalies was 14.1 per cent (48 cases). However, the incidence of anomalies after virus disease in the first trimester was about 21 per cent—a risk of about 1 in 5 cases.

Table VI records the first trimester virus diseases and their respective incidences of congenital anomalies.

TABLE VI. COLLECTED INCIDENCE OF ANOMALIES FOLLOWING FIRST TRIMESTER VIRUS DISEASE
OTHER THAN RUBELLA

DISEASE	TOTAL	ANOMALIES	ABORTIONS
Measles	26	7	1
Mumps	45	9	2
Varicella	8	2	0
Infectious mononucleosis	7	3	0
Influenza	4	4	0
Poliomyelitis	63	4	8
Virus pneumonia	1	1	0
Totals	154	30 (20.9%)*	11 (7.1%)

*Excluding abortions.

Comment

We have shown that virus diseases other than rubella can and do cause fetal anomalies. However, these diseases do not result in a definite pattern or syndrome of anomalies as does rubella, nor do they result in anomalies with as great a frequency as does rubella. The chief difficulty in attempting to establish an accurate or significant expected incidence of anomalies is the task of assembling a large enough series of cases. Whereas there exists in the literature a large series of cases of rubella in pregnancy, only a comparatively few cases of other virus diseases complicating pregnancy have been collected. The expected incidence of anomalies following rubella has been revised with the increasing numbers of cases from the previously reported 100 per cent to the latest figure of 40 per cent risk. The reports of Swan, Gregg, and others resulted in widespread interest in this subject. The unusually virulent epidemics of rubella affecting young adults in Australia resulted in an extremely high incidence of fetal anomalies; these anomalies conformed to a definite pattern. The high incidence reported is not entirely accurate in that the authors were not able to ascertain the number of normal infants born to mothers having rubella in early pregnancy. While the collected series of virus diseases in the first trimester consists of no less than 154 cases, there is an incidence of slightly more than 20 per cent fetal anomalies. This shows a definite increase over the expected incidence of anomalies in a comparable un-complicated series (about 1 per cent). If in the future a larger series is accumulated, there will no doubt be a downward revision of expected incidence, but we feel that even so it will be greater than in uncomplicated pregnancies.

As we have stated previously, even though virus diseases in early pregnancy cause an increase in fetal anomalies, these diseases play only a small role in the over-all etiology. We found only 1 case of measles, 1 of rubella, 3 of influenza or "virus X," 1 of virus pneumonia, 1 of severe upper respiratory infection (a total of 7 cases of acute virus disease in the first trimester) in our entire series of 273 congenital anomalies at Michael Reese Hospital.

Studying our series further, we have confirmed the work of Burge and have shown that bleeding or threatened abortion in early pregnancy does not increase the incidence of fetal anomalies. Burge found an 8.6 per cent incidence of history of threatened abortion in 289 cases of congenital anomalies whereas we found a 9.2 per cent incidence. He showed conclusively that threatened abortion will not cause a significantly increased number of congenital anomalies in viable children regardless of treatment. There were only 25 cases in our series, an average of 5 cases per year. Certainly there was a much greater number of cases of threatened abortion which resulted in normal children each year. We could find no correlation between the incidence of chronic maternal disease and the occurrence of fetal anomalies although it is conceivable that maternal debilitation could disturb the placental nutrition and cause fetal anomalies. In only 9 of our 273 cases were we able to demonstrate a hereditary factor in the etiology of the anomalies. However, our questionnaire did not adequately delve into this problem.

Although we discovered possible etiological factors in the prenatal histories in 90 of our 273 cases, we must admit that many of the former could not possibly have affected the fetal development, particularly in those illnesses or bleedings which occurred after the first trimester. Therefore, we must conclude that even greater study must be made in order to find preventable etiological factors. The thought-provoking theory of fetal infection in an immune mother as postulated by Schick merits further investigation. While we were unable to ascertain any cases similar to those of Warkany (as quoted by Schick) and Hagströmer, this is entirely understandable in view of the fact that many women could not remember simple exposure to a virus disease. In addition, many women would not even remember any illnesses which may have occurred during their pregnancies.

There is a large amount of experimental work being performed at the present time on the various etiologies of fetal anomalies. Although this work is being done with laboratory animals, a great deal can be drawn from it by inference. Warkany's[33] monumental experiments on the results of maternal vitamin deficiencies are perhaps most widely known. We cannot transpose this work to our series of patients since it would have been impossible to have determined their dietary status during early pregnancy. Hamburger and Habel[34] have shown a definite teratogenic effect on chick embryos by the mumps and influenza viruses, although there is no pattern as with rubella. Ingalls and co-workers,[35] in experiments on mice, have shown that lowered oxygen tension with resultant maternal and fetal hypoxia caused an increased incidence of defects. By varying the stage of gestation when the maternal insult occurred or by varying the degree of hypoxia, the number, type, and degree of fetal defects were directly changed. This might be projected to the human being by postulating fetal defects following hypoxia due to defective placentation or the compromising of placental circulation and nutrition by various maternal illnesses or noxious agents.

In conclusion, the problem of the effects of virus diseases on the unborn fetus will not be solved until all cases of such diseases and their outcome are regularly reported and assembled by a central agency. A statistical analysis will be valid, and the expected incidence of anomalies can be determined, when this event shall occur.

Summary and Conclusions

1. From a review of the world literature, a series of 154 cases of virus disease in early pregnancy, other than rubella, has been compiled.

2. An incidence of 21 per cent fetal anomalies was found following these virus diseases in the first trimester of pregnancy. This is compared to the 40 per cent incidence of anomalies following rubella.

3. Bleeding or threatened abortion does not appear to increase the incidence of congenital anomalies.

4. Considering fetal abnormalities as a whole, virus diseases per se play only a small role in etiology.

5. Chronic maternal illnesses do not constitute a threat to normal fetal development in the vast majority of cases.

6. Much greater study of the problem of congenital anomalies is needed by clinical, statistical, and experimental laboratory methods.

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Discussion

DR. STANLEY GIBSON.—I have only one excuse for discussing this very important paper: I am interested in the problem of congenital heart disease and we know that if the mother has had German measles in the first trimester of pregnancy the baby is likely to have congenital heart disease.   Wesselhoeft gathered from the literature 521 cases, in which 221 had eye defects, 243 had hearing defects, and 221 had congenital heart disease.   While it is generally agreed that congenital heart disease is a frequent part of this picture, I was not able to find in the literature any statement as to the sort of cardiac disease these children had.   Therefore, at the Children's Memorial Hospital, Dr. Lewis and I undertook a study which consisted of 1,366 cases of congenital heart disease.   In each case the mother was very carefully questioned not only as to rubella but regarding other diseases during preg-

nancy. In this entire group of 1,366 we encountered only 17 instances where the mother gave a history of German measles during pregnancy, and all but one had been in the first trimester.

Our findings were most interesting. Of these 17 cases, 14 of the babies had patent ductus arteriosus, one was thought to have an auricular septal defect, one a ventricular septal defect, and only one of the 17 had cyanosis, a typical picture of the tetralogy of Fallot. Of the 14 cases of patent ductus arteriosus, 10 were proved by operation so we have evidence of the correctness of the diagnosis. There were 4 other cases with typical clinical symptoms.

There was another thing that interested us. Of the 10 children operated on for patent ductus arteriosus, 4 had some accompanying lesion. One had pulmonary stenosis, one had coarctation of the aorta which was excised along with the ductus. Two had persistent murmurs that indicated what we thought was a septal defect after a patent ductus had been closed. So 4 out of the 10 apparently had an additional lesion. In other words, even though patent ductus seems to be the predominant lesion in these children, from our small series we conclude that some complicating lesion is more frequent in these children than in patent ductus where the mother has not had German measles.

German measles in the mother is not an important cause of congenital heart disease. Only in slightly over 1 per cent of our cases of congenital heart disease do we find a history of German measles in the mother, but when it does occur it is of tremendous importance. I do not know whether all of you have seen these German measles babies. They present a most pathetic picture. Perhaps I should not give advice to obstetricians but, from what I see of these children, I feel that if a diagnosis of German measles is made in the mother in the first two months of pregnancy, abortion is certainly justified.

A METHOD OF FORCEPS ROTATION IN PERSISTENT OCCIPUT POSTERIOR*

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IN REFERRING specifically to the management of occiput posterior, Dr. Edmund Piper once said that "in our service we do not advocate any one particular way of doing anything."[1] He then continued: "I would like to go on record as feeling that there are at least two ways of doing anything, and if I do it one way I am not criticizing someone else for doing it another way." It is in this spirit that the present paper is presented. These remarks should not be construed as suggesting that the technique to be described is in any way superior to other methods of forceps rotation, or to the more generally employed manual rotation. It is merely a technique which I personally prefer, for the reason that in my hands it has proved simpler, and it is safe and effective. It has been used to the exclusion of other methods over the course of the past twelve years. A preliminary description[2] of this rotation was published in 1946, based upon an experience of approximately fifty deliveries in which it was employed. Since this time the operation has been used 62 times.

In order to clarify the procedure to be described, it is necessary to review briefly the major techniques which are now employed. Forceps rotation in occiput posterior may be accomplished by Kielland forceps; by classical forceps employing the so-called "double application" for delivery; or by DeLee's "key-in-lock" maneuver. The technique of double application of the forceps is typified by the modern concept of the Scanzoni extraction. In this procedure a classical forceps is applied to the sides of the head with the concavity of the pelvic curve looking toward the face of the child. Rotation and traction are applied simultaneously, resulting in spiral advance of the head. When the occiput reaches the anterior position, the forceps is removed, and reapplied to the anterior position for delivery. In the interest of historical accuracy, it should be mentioned that our modern concept of Scanzoni's rotation[3] bears little resemblance to the original description of this operation.[4] As originally described, the rotation is carried out at the level of arrest without traction. Also, the first movement rotates only to the transverse position, at which point the forceps is removed and reapplied for completion of the rotation. In Bill's[5] rotation, which also employs double application, the Tucker-McLane forceps is used. The rotation from posterior to anterior position is carried out by a single sweeping movement immediately upon full dilatation of the cervix,

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and in precisely the pelvic plane in which the head is found at the time. The only stipulation as to station is that the head be "in the pelvic cavity." In DeLee's key-in-lock maneuver, the forceps is applied as for the Scanzoni. The head is now lifted off the point of arrest, and rotated through only a short arc. The forceps is now released, wandered back to the original position in the pelvis, and caused to seize the head obliquely, as with one blade over the anterior brow and the other over the posterior mastoid region. The head is now elevated again, and rotated through a second short arc. By a series of such maneuvers, the position ultimately reaches the occiput anterior.
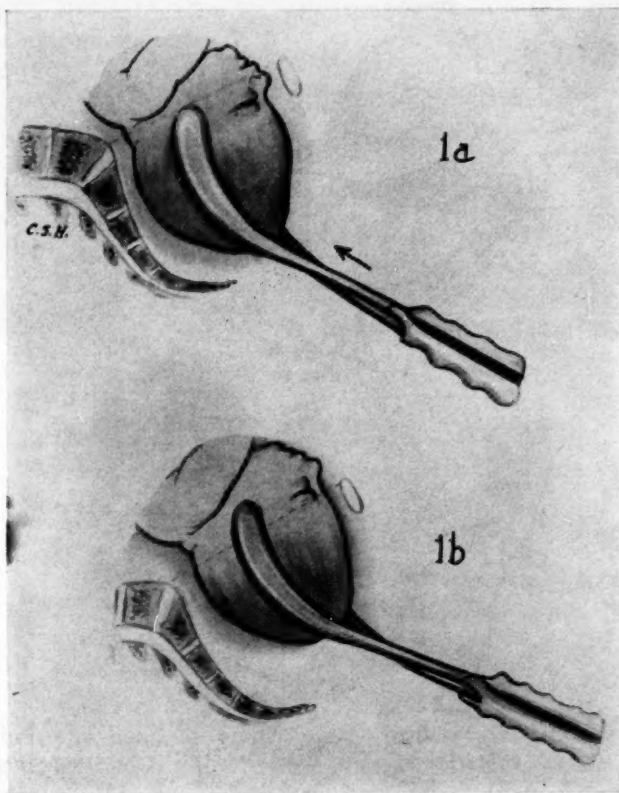
Fig. 1.

The present technique, described before[2] as the Stillman procedure, combines the simplicity of the Bill rotation with DeLee's concept of intermittent rotation above the level of arrest. The various steps in the procedure are the following:

First: A Tucker-McLane forceps, which is preferable for the rotation, is applied by an accurate cephalic application to the posterior, the concavity of the pelvic curve looking upward toward the face of the child. Since partial deflection attitudes are common in persistent posterior, the handles of the forceps are depressed slightly before locking. The instrument is then locked.

Second: The head is gently pushed upward in the birth canal above the level of arrest. This elevation is generally continued until an outpouring of amniotic fluid occurs from the introitus, this signifying that the head has been sufficiently elevated that easy rotation can be accomplished (Fig. 1).

Third: Holding the head at this slightly higher level, the handles of the forceps are then raised as in Fig. 2. This is done in order that the tips of the forceps blades may be centered in the birth canal, and the blades themselves centered in the axis of the vagina. This position of the forceps constitutes the point of origin of the rotation. In subsequent movements the forceps handles describe a wide arc such that the blades do not deviate from this original axis.

Fig. 2.

Fig. 3.

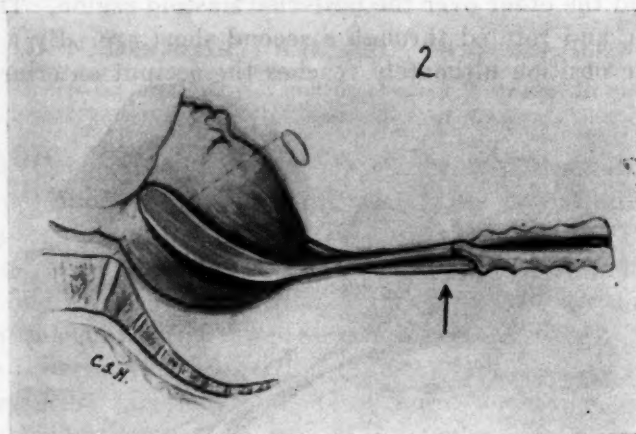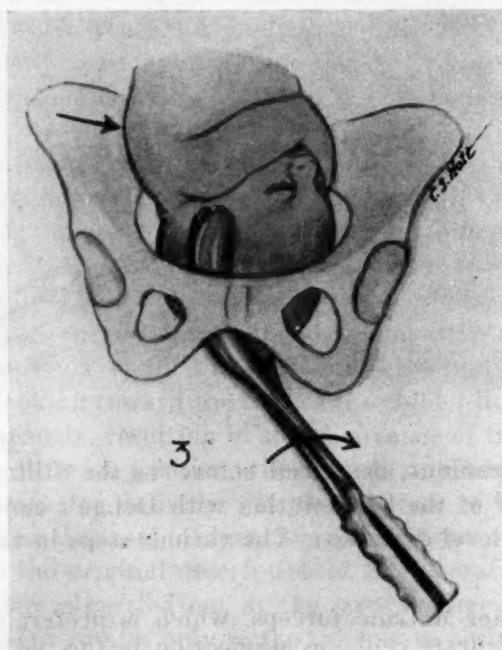*Fourth:* With the handles raised, and the head held at this slightly higher station, the handles are caused to sweep through an arc of 15 to 30 degrees only, thus causing the head to rotate an equivalent amount. As the head rotates through this short arc, it tends (or is allowed) to descend slightly, returning again to the level of arrest (Fig. 3).

Fifth: The head is again elevated above the level of arrest from this new position, and again rotated through a 15 to 30 degree arc, at the conclusion of which it tends to return once more to the level of arrest. By a series of such maneuvers (elevation slightly above the level of arrest, and rotation through a short arc with return to the level of arrest), rotation to the anterior position is ultimately accomplished.

The above steps should be carried out with the utmost deliberation and the greatest gentleness, and should properly require at least one minute's time. If any resistance whatever is encountered, or if the fetal heart gives evidence of embarrassment, the head should be returned to its original position and rotation carried out in the opposite direction. During the various steps in the rotation, it is desirable for an assistant to move the anterior shoulder across the lower abdomen.

Fig. 4.

Sixth: When the head reaches the occiput anterior position, the forceps handles, having described a wide arc, now point toward the floor, and the concavity of the pelvic curve looks toward the sacrum (Fig. 4). Slight traction is now made for the purpose only of fixing the head in its new position.

Seventh: The left blade of the rotating forceps, now lying upon the *right* side of the mother's pelvis, is removed and is replaced by the right blade of the Simpson forceps. The right blade of the rotating forceps is now removed, and is replaced by the *left* blade of the Simpson forceps. Both blades of the rotating forceps should not be removed at once; leaving one blade in place at all times tends to prevent the head from rotating back to the posterior position.

Eighth: Since the right blade of the Simpson forceps has been applied first, it is necessary that the handles be rearranged for locking. This is done, the forceps is locked, and extraction is accomplished with intermittent traction, as in any midforceps delivery.

Results

Of the cases in which this procedure was used prior to 1946, specific details are not available. According to my recollection there were no birth injuries, nor did any of the cases offer particular difficulty. Among the last 62 cases,

there were no infants injured, and there were no vaginal or cervical lacerations resulting from the procedure. There was one cord prolapse in a case in which it was necessary to disengage the head in order to accomplish rotation; immediate version and extraction were done and the child showed no embarrassment. In three cases much difficulty was encountered with the rotation of the shoulders, this being attributed to tonic contraction of the uterus resulting from spinal anesthesia. Two of these cases were ultimately successful. In the remaining one, although the head was easily rotated in either direction, the fetal heartbeat became irregular as soon as the anterior position was reached. The posterior sagittal segment at the outlet was fortunately long, and face-to-pubes delivery was accomplished without further incident.

Comment

A fundamental requisite of any technique for rotation is that it be safe for both mother and baby. The absence of birth injury or soft tissue laceration suggests that the present technique satisfies this requirement. A second requisite is that the procedure be reasonably simple. This also appears to be satisfied, as the technique is very readily grasped by residents and interested interns, and is carried out by them with ease and safety. Finally, it should be as effective as other acceptable techniques. Comparison with a series of cases of manual rotation suggests that this requirement, too, is satisfied. Among 86 cases reported by W. C. Danforth[6] in which manual rotation was attempted, there were 76 successful cases; there were 9 cases in which manual rotation was attempted and failed of success; and there was one case of prolapse of the cord which was successfully managed by version and extraction.

Although this paper does not deal with indications or conditions, it is emphasized that unless there is specific contraindication, one should allow a full second stage of labor before intervention. By so doing the majority of posteriors will rotate spontaneously. In those which persist as posterior, the presence of maximum descent and maximum molding greatly minimizes the hazard of rotation.

Among the difficulties which may be encountered are: slipping of the head within the forceps; encountering of resistance as the rotation proceeds; and inability to cause the shoulders to rotate. The first of these, slipping of the head within the forceps, may be serious only when one does not realize that it has occurred. One may easily perceive such slipping by placing the left index finger against the scalp during the rotation; and in any event one must carefully check the position before removal of the rotating forceps. The second difficulty, the encountering of resistance however small, suggests that the head has not been elevated sufficiently to allow easy rotation. If similar resistance is encountered with slight further elevation one should then return the head to its original position and rotate in the opposite direction. Under no circumstances should the rotation be carried out against resistance, nor should it be carried out with haste except in the most extreme emergency. The final difficulty, failure of the shoulders to rotate, is ordinarily due to inadequate relaxation of the uterine musculature. The three cases in which this was encountered were all attributed to the enhanced uterine tone which

follows spinal anesthesia. Although this is generally not troublesome, nevertheless it emphasizes the fact that inadequate uterine relaxation may cause serious difficulty in the performance of any intrauterine manipulation. For this reason, inhalation anesthesia, with proper preanesthetic medication, is considered the anesthesia of choice for this, as for other rotations from the posterior. The rare complication of cord prolapse must, of course, be dealt with by version and extraction. Such an operation is unthinkable under spinal anesthesia.

No mention has been made of the cervical and vaginal lacerations which are sometimes attributed to forceps rotation. The first of these may be avoided by awaiting full dilatation and retraction of the cervix before intervention. Vaginal laceration does not occur if the forceps blades are properly centered in the axis of the vagina before the rotation is begun, and are not allowed to deviate from this axis during the various steps in the rotation.

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Discussion

DR. RALPH A. REIS.—There are many ways of managing persistent occipitoposterior. I want to compliment Dr. Danforth for calling our attention to another method. The simplest method is the old long black cigar which you smoke slowly while the occipitoposterior rotates. Another is the Hodge maneuver, an almost forgotten method of flexion of the head, which overcomes the deflexion and permits rotation. Many are just delivered as persistent occipitoposteriors in spite of the fact that a well-trained obstetrician of this city has declared that anyone who delivers a persistent occipitoposterior as such is guilty of mayhem and malpractice. Then there is the principle which depends on the dislodgment of the head and rotation.

Dr. Danforth mentioned many methods of instrumental rotation—the Scanzoni, both single and double blade, the key-in-lock maneuver, and the Veit maneuver. This new method I find somewhat difficult to understand without having tried it. He said it is very simple and its technique is readily grasped by residents and interns. Being neither, I suppose that is part of my difficulty. One point Dr. Danforth did not stress sufficiently in my opinion was the attempt at correction of the deflection which is always present in persistent occipitoposterior and which correction, it seems to me, is the sine qua non of the treatment of occipitoposterior. Without the correction of the deflection an occipitoposterior is not properly handled. He said the head should be pushed out of the pelvis after the forceps is applied until there is a gush of amniotic fluid alongside the forceps. I can think of many patients in whom I would have to keep pushing until doomsday and there would be no change, because there is no amniotic fluid to gush. It seems to me that rotation is easier and it seems to me it is much easier to continue rotation than to stop at 15° and repeat the procedure four or five times. He says if the fetal heart tones show embarrassment the head should be brought back to its original position and rotated to the other side. May I simply suggest that if the fetal heart tones become irregular, the procedure be stopped. I agree

that for this procedure it is necessary to use deep inhalation anesthesia. Dr. Danforth says the method he uses is successful and safe. This I cannot deny. He says it is simple. This I must continue to question. When he says it is as effective as any other method, I wonder whether this is a fair conclusion since he has not used any other method in the last twelve years.

DR. GEORGE B. BRADBURN.—The procedure described by Dr. Danforth in this paper has been my method of choice in the handling of occiput posterior positions for the past five years. I would estimate that I have used it well over fifty times, although I have not analyzed my own records. I agree that it is simple and safe. I have encountered no fetal injuries that could be attributed to its use. I believe that in a few of the more difficult higher rotations, lacerations over the spines have resulted from forceps trauma.

Most times cyclopropane anesthesia has been used for the operation, although a considerable number have been successfully done with pudendal block. I have had the experience, on a number of occasions when pudendal block was used for the rotation, that, after it had been accomplished, the head would descend quickly and spontaneous delivery follow.

This procedure is naturally easier in a multiparous woman, and often saves a prolonged second stage in a patient who is making no progress after complete dilatation. These are the patients in whom I have attempted to teach our residents the technique of rotation. They all grasp it readily. One of the reasons this method has been popular with me, perhaps, has been the fact that no one adequately taught me any method of rotating during my training period. I have always been squeamish in the handling of a fetal head by manual means, and I believe I am less traumatic to the fetus by using the forceps.

The implication in this paper is that this procedure is used in treating the arrested occiput posterior. My feelings are that the indications for delivering an occiput posterior as such are rare. Many times the head will descend to a low station as an occiput sacral. Delivery without rotation adds a great strain on the mother's perineum. This same rotation can be done with a head crowning and with only a small amount of elevation of the head needed to accomplish it.

Another situation in which this procedure has helped me has been in the handling of a deep transverse arrest. I am sure you all have had difficulty in either manually rotating to the anterior or applying Kielland forceps. Most times a simple manual rotation to a direct occiput sacral is easily accomplished. Cephalic application of forceps and rotation from this point are usually successful. If resistance is encountered after rotation has reached the transverse, traction to bring the head to a lower station without further rotation will usually allow completion of the rotation when the head reaches the pelvic floor. This type of pelvis is mechanically adapted for descent in the transverse, and attempts to change the natural mechanism are too traumatic to both mother and baby.

DR. DANFORTH (Closing).—I wish to thank Dr. Bradburn for his remarks, and am pleased to find that his experience parallels my own. Dr. Reis asked two questions, first, the reason why the head could not be elevated, and complete rotation accomplished in one movement with the head at this elevated station. By elevating and rotating only through a short arc, the only real force expended on the head is that of elevation. The force required for the short rotation is negligible. Accomplishing the entire rotation in one movement requires an expenditure of force upon the head which in my opinion is undesirable. Dr. Reis also asked how I know that this rotation is as effective as manual rotation. I did not say that it is. I did say that in my hands the procedure works satisfactorily and is safe. I would certainly not suggest that I can do this better than Dr. Reis can do manual rotation. I do say, however, that I personally am able to do this forceps rotation better than I can do manual rotation.

VAGINAL BURNS FROM POTASSIUM PERMANGANATE

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WITHIN the last few years, a new minor problem has appeared in American gynecology. The use of mild solutions of potassium permanganate, as douches, is not new. But the insertion of tablets of this chemical compound into the vagina to "bring down the period" is a rather recent phenomenon, and it is rapidly finding favor as an abortifacient, futile though it may be.

In 1945, fourteen French and Italian reports on the use of this drug, dating from 1932 to 1945, were summarized by Simard.[1] Frullani[2] says that the treatment of vaginal burns of this type, usually from attempted self-induced abortions, has been an old problem in Italy. De Bacalao[3] reports that the use of potassium permanganate is common among the poorer classes and the prostitutes in Venezuela.

The earliest American report came from Boston in 1941, with the first case recorded there in 1936.[4] This report was brought up to date in 1945 by McDonough[5] and totaled sixty-five cases. Two other reports have been published more recently, one from New Orleans,[6] and one from Brooklyn.[7]

The first known case appeared at Bellevue Hospital in December, 1942, and occasional cases were subsequently seen in 1944, 1946, 1947, 1948, and 1949. In 1950, however, five cases were seen, and in 1951 nine of these chemical burns of the vagina were cared for. Three additional cases, not included in this series, appeared in January, 1952. The incidence is obviously rising sharply.

Since most of the twenty cases here summarized were caused by attempts at self-induced abortions, a sense of guilt often forced a patient to postpone the seeking of medical aid, and to tell false stories to the admitting physician when the aid was sought. The truth was often disclosed only by the vaginal speculum, and one of these women steadfastly denied using a tablet even when the remains of one was removed and held before her eyes. Others admitted only to taking douches of potassium permanganate solution, even though the vaginal lesions were the typically sharp-edged blackened craters that result from the tablets.

This latter story is probably true on occasion, since the 0.3 Gm. tablet commonly used may require as long as twenty-five minutes to dissolve completely in two quarts of agitated warm water, and a woman who drops a tablet into her douche bag may be burned by the undissolved fragments in her douche.

Four of these twenty women arrived at Bellevue in shock, a fifth in impending shock. All five received at least 500 c.c. of whole blood in each case, and one of these, whose case is reported here in detail, received 1,500 c.c. Intravenous fluids were freely used in many of the twenty cases.

Fresh vaginal bleeding, resembling that of an abortion, was the usual finding, and three of these women were treated initially as having abortions, a hasty pelvic examination mistaking a parous cervix for an open one. Seventeen of our patients were parous, with from one to six deliveries. Careful speculum examination was needed, as a rule, although a deep crater was sometimes felt. We found that the open speculum might cover the crater, or its pressure temporarily stop an eroded vessel from bleeding, so that the speculum position had to be altered and the speculum partly closed to assay the situation completely. A cursory inspection would easily miss a bleeding point.

Potassium permanganate tablets will produce lesions varying from areas of scorched brown mucosa to punched-out craters, most often in the vaginal fornices or on the cervix. The size and depth of the lesion will depend upon the elapsed exposure time. In this series, bleeding occurred anywhere from three to twenty hours after placement of the tablets. The degree and onset time of heavy bleeding will depend upon the size of the eroded blood vessels. Craters from 2 to 7 cm. in diameter were found in these cases, but the heaviest bleeding was not necessarily related to the largest lesions. As the detailed case showed, moderate ooze from a fresh burn could turn into active bleeding once sloughing had occurred, and a delayed hemorrhage result.

Treatment varied from observation at bed rest to suture ligation of bleeding points plus vaginal packs. Oxycel, petrolatum gauze, and plain gauze were all used by various operators. Of these twenty, six received both ligation and packs, four had ligation only. Three of these four signed out of the hospital as soon as the suture work was finished. Seven cases were controlled by vaginal packs alone, and the bleeding stopped spontaneously in three when the permanganate tablets were removed.

Seventeen of these women were probably trying to interrupt pregnancies, their menses being overdue anywhere from one day to five months. Only twelve were diagnosed as pregnant. One woman tried a tablet for the relief of Trichomonas vaginitis. A second used a postcoital permanganate douche, and had a typical blackened crater on the cervix, apparently from a fragment of a tablet passing through the tubing and lodging in the vagina. A third woman was given a tablet by her sex partner for her to place in order to "avoid infection."

In no instance did abortion occur. One woman returned two months later with an open, bleeding cervical os and a triumphant smile, having successfully tried some other method the second time. Six of these women were subsequently delivered at Bellevue, four of normal term babies, one of a normal premature infant, and one of a premature hydrocephalic monster. In 1949, a Bellevue patient who had had permanganate burns treated elsewhere, pre-

viously, was delivered by cesarean section because of the extreme scarring and stenosis of the cervix and upper vagina that had resulted. This represents the worst sequelae we have encountered in these cases of burns.

Ten of the twenty women were immigrants from Puerto Rico. Two were of Negro blood and eight of European descent. Three of the latter were of Italian ancestry. Fifteen were legally married, three single, one separated, and one widowed, varying in age from 18 to 38 years.

The most serious case in this series is here presented.

R. W., 27-year-old married Negro woman, menses seventy-five days overdue, was admitted in shock at 4 A.M., with heavy vaginal bleeding of twelve hours' duration. The bleeding had begun eighteen hours after placing four permanganate tablets in the vagina. She was gravida vii, para vi, with 4 children alive and well.

The vaginal speculum showed ulcerations of the cervix and both lateral fornices of the vagina. Much of the vaginal mucosa was browned or blackened. The uterus was soft and the size of a ten weeks' pregnancy.

Shock was treated with 250 c.c. of plasma, 1,500 c.c. of intravenous glucose solutions, and 1,000 c.c. of whole blood. The urine was concentrated, and after this treatment the hemoglobin was 12 Gm., and the red blood cell count 4.1 million. Blood type was B, Rh positive, and the Mazzini test was negative.

The vaginal bleeding was controlled by a dry gauze pack. Thirty-six hours later this was removed and the bleeding points suture ligated, with an Oxycel pack again placed in the vagina. The second pack was removed after forty-eight hours, and vaginal inspection showed oozing necrotic ulcers, but no active bleeding points. Within six hours she was again in shock, and bleeding vaginally. One thousand c.c. of intravenous fluid and 500 c.c. of whole blood were given, and the vagina was packed for the third time. This pack was removed four days later without incident and the patient was discharged after a total hospital stay of thirteen days. Her course was afebrile on prophylactic penicillin therapy.

Two months later she was admitted to the hospital from the prenatal clinic, and sent to the surgical division with jaundice, anorexia, and right upper quadrant pain. Her pregnancy was proceeding normally, and the vaginal lesions were healing. A tentative diagnosis of acute cholecystitis was changed to that of homologous serum jaundice, and confirmed by laboratory tests. She was transferred to the medical service for four weeks, and developed vaginal spotting just before time for her discharge. Diagnosis of threatened abortion was made, and she was transferred to the gynecological wards. After two days the vaginal spotting ceased and she was discharged from Bellevue.

Two months later she was admitted to the maternity wards, and was delivered of a 3 pound, 2 ounce male infant. This child has done well, and his mother is very happy with him.

Eventually this patient disclosed that she had learned of the new "way to miscarry" from a British war bride, and had spread the news until her own trial of the tablets cured her of her belief.

Conclusions

1. Direct introduction of potassium permanganate tablets into the vagina, usually as an abortifacient, is in increasing use among American women.

2. Severe vaginal damage and dangerous hemorrhage may result.

3. Treatment consists of control of the bleeding by the simplest possible method, and the replacement of the blood loss, if necessary.

4. The lay belief in the efficacy of this drug apparently stems from Europe and South America.

5. Efforts to discredit its use should be made.

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THE CLINICAL FINDINGS IN THE PRESENCE OF SYRINGOSPORA ALBICANS AND STELLATOIDEA

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IN A searching inquiry Conant[1] claims that the name Syringospora, suggested by Quinquaud in 1868, was the first validly published genus for the organism of moniliasis. Others[2,3] are of this same opinion and we wish to employ this generic name in conformity with the established laws of priority.

The purpose of this paper is to cite the incidence of three Syringospora species in the vaginal discharges of pregnant women and to study any association of symptoms with their presence.

Materials and Methods

Saline suspensions of the vaginal discharges of regularly attending Negro prenatal patients were examined immediately for the presence of yeastlike organisms and trichomonads. The only other criteria used in the selection of patients for this study were the presence of the pseudomycelia by direct examination in the fresh-mount preparations and the absence, on routine prenatal examination, of other conditions or factors likely to cause pruritus or vaginitis. Those with positive cases were questioned indirectly as to symptoms and observations were made of the local findings.

The method of Martin and associates[4,5] was followed for the identification of the species. One positive identification was obtained for each patient so that mixed infections were not determined.

Results

One hundred fifty patients were studied and the species of Syringospora identified. Eighty-two, or 54.7 per cent, harbored *S. stellatoidea* and 66, or 44.0 per cent, showed *S. albicans*. From 2 asymptomatic patients *S. tropicalis* was cultured, and because of its infrequent occurrence it was not included in the analysis of the results.

Pruritus was found in 55 per cent of the remaining 148 infected persons, that is, in 35 of the 82 individuals harboring *S. stellatoidea*, in 46 of 66 patients infected with *S. albicans*.

There were 67 asymptomatic patients infected with these same species. Of these, 47 (70.1 per cent) showed the presence of *S. stellatoidea* and 20 (29.8 per cent) showed *S. albicans* (Table I).

A diagnosis of vulvovaginitis from the local findings was made in 43 individuals, or 29 per cent of all patients. These patients presented the classical picture on vaginal examination. Of 17 such patients with *S. albicans* 12, or 70.6 per cent, complained of pruritus and 15 (57.7 per cent) of 26 patients infected with *S. stellatoidea* had pruritus.

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Comment

The above data show that the presence of Syringospora in the vagina does not indicate coincidence of symptoms. This is a not infrequent clinical observation and was emphasized by Plass and collaborators[6] in their studies. Jones and his co-workers[5,7] believe that many of the yeastlike fungi formerly identified as *S. albicans* may prove to be *S. stellatoidea*. They report *S. albicans* from 91.07 per cent of patients with a chief complaint of pruritus vulvae referable to a mycotic vulvovaginitis. In their group of 251 white and 29 Negro patients (91 pregnant and 189 nonpregnant), only 6.78 per cent harbored *S. stellatoidea*. In contrast to this work, Johnson and Mayne[8] found no definite relationship of symptoms with any species of yeast. However, they conclude that their results are in general agreement with the work of Carter and associates,[9] who found that *S. albicans*, *S. stellatoidea*, and *S. tropicalis* are associated with symptoms while the other yeasts are not.

Various and multiple factors are stressed by different observers as producing symptoms in some individuals and not in others harboring the same species. Johnson and Mayne[8] show a definite correlation between the quantitative degree of infection with yeasts and symptoms. However, in the present study 29.4 per cent of patients with *S. albicans* and 42.3 per cent with *S. stellatoidea*, presenting the classical picture on vaginal examination, were asymptomatic. In these cases both individual sensitivity and contact between the cutaneous areas and the discharge seemed to play a role in setting up the mechanism whereby the pruritic symptom was produced. The numerical distribution of this vaginitis shows no significant difference from one which would be obtained by chance.

TABLE I. THE ASSOCIATION OF SPECIES ISOLATED WITH PRURITUS VULVAE

	TOTAL	PATIENTS WITH S. ALBICANS	PATIENTS WITH S. STELLATOIDEA
Total	148	66	82
Patients with pruritus	81	46	35
Patients without pruritus	67	20	47

$$p = < 0.01$$

In interpreting the results of this study a statistical evaluation of all data was made. A difference was considered significant only when the probability of its occurring by chance alone was less than 1 in 100. Table I shows a very significant degree of correlation existing between the species of yeastlike fungi isolated and the pruritic symptom. The percentage of pruritus among the patients with *S. albicans* is 70 per cent, while the percentage of pruritus among patients showing *S. stellatoidea* is 43 per cent. The percentages are statistically highly significantly different (probability less than 0.01).

Clinically no definite statement can be made of the species of Syringospora present in patients with pruritus vulvae. This is true in the presence or absence of a typical mycotic vulvovaginitis. Furthermore, the relative pathogenicity of the different species appears to depend on the sensitivity of the individual and

other predisposing factors such as the trimester of pregnancy and glycosuria. However, the present study reveals that the symptom of otherwise unexplained pruritus is associated significantly with the presence of *S. albicans*. Conversely, lacking this symptom the patient's culture is more likely to show *S. stellatoidea*.

Summary

1. Of 150 pregnant Negro patients showing the presence of pseudomycelia by wet-mount examination, 44.0 per cent harbored *Syringospora albicans*, 54.7 per cent had *Syringospora stellatoidea*, and *Syringospora tropicalis* was present in 2 cases.

2. Forty-three, or 29 per cent of all patients, revealed the classical picture of a mycotic vulvovaginitis. No definite correlation between the occurrence of this picture and the incidence of the species was found.

3. Pruritus vulvae was present in 55 per cent of all infected patients. Sixty-six patients were positive for *S. albicans* and of these 46 complained of pruritus vulvae while only 35 of 82 patients with *S. stellatoidea* were likewise positive.

4. Of 67 asymptomatic patients only 20 harbored *S. albicans*, whereas 47 showed positive cultures for *S. stellatoidea*.

5. It is not possible to make a clinical diagnosis of the species of Syringospora present in mycotic vulvovaginitis, with or without pruritus vulvae. However, the pruritic symptom is related significantly to the presence of *Syringospora albicans* and not to *Syringospora stellatoidea*.

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THE INTERPOSITION OPERATION

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THE object of this report is to demonstrate that the criticisms leveled at the interposition operation are by no means fully justified. The hue and cry raised against this procedure, in many instances by those who have never performed the operation, bid fair to relegate it to oblivion. This procedure is far too useful to be permitted to suffer such a fate.

The interposition operation, also called the transposition operation, is one in which the uterus is interposed between the bladder and the anterior vaginal wall, the uterus forming a shelf on which the bladder rests. The uterus is pulled forward after the bladder has been freed from its attachments to the vagina and uterus. The bladder is placed on the posterosuperior surface of the uterus, after which the uterus is fixed on each side to the tissues on the posterior surface of the pubic rami close to the pubic arch. By this maneuver, one is enabled at one and the same time to correct a cystocele and any displacement or prolapse of the uterus of whatever degree.

To whom belongs the honor of first describing this operation is a question which has been argued at length and in numerous publications and at this late date, over half a century since its first description, suffice it to say there is glory enough for all who contributed to the development and perfection of this procedure. We are indebted to Watkins,[1] who first performed the operation in January, 1898, and published it in November, 1899, to Wertheim,[2] who described a similar technique in 1899, and to Schauta,[3] Freund,[4] and Fritsch,[5] each of whom supplied an addition which improved the efficiency of the operation.

Technique

Before proceeding with the interposition proper, the endometrial cavity is curetted and, should the tissue obtained arouse a suspicion of malignancy, the interposition operation is abandoned. The treatment is either delayed or another method of dealing with the condition is chosen.

Following the curettage, the cervix is pulled downward and forward and a transverse incision is made on the anterior surface of the portio just below the lower border of the bladder. A vertical incision may then be made from the center of the transverse portio incision, extending upward in the vaginal mucosa, and the bladder is then freed by blunt and sharp dissection from the mucosa medially and laterally up to a short distance beneath the urethra. The bladder is then freed from the parietal peritoneum by a similar method of dissection.

I find it more convenient after making the transverse incision to free the bladder first posteriorly by blunt dissection with the scalpel handle and the gauze-covered finger, and then to free it anteriorly from the vagina by a combination of finger, gauze, and some sharp dissection. This method expedites the mobilization of the bladder, the exposure of the anterior parietal cul-de-sac, and also seems to reduce the amount of blood loss. To avoid urinary symptoms arising from displacement of the bladder and uterus it is advisable to free the bladder completely. The bladder pillars should be cut, the bladder freely mobilized and converted into an abdominal organ. This eliminates sacculation with its attendant frequency and dysuria.

After the bladder is mobilized, a Sims speculum is introduced between it and the peritoneum of the anterior cul-de-sac and pressure is exerted in an upward and backward direction by an assistant. This removes the bladder from the immediate field of operation and permits the ready recognition of the peritoneum. The glistening peritoneum is grasped by a tissue forceps or a clamp and is cut with scissors. The Sims speculum, which has been keeping the bladder out of the field, is now introduced into this incision. At this point some surgeons place a suture in the upper margin of the cut peritoneum, and leave it long so as to facilitate its recognition.

Traction on the cervix is now greatly diminished or abolished and the corpus is brought to or even out of the wound and inspected. This is accomplished by progressively grasping the corpus at higher levels with volsella or cat's-paw retractors. Whatever pathology is encountered is dealt with and, in women who still menstruate, tubal sterilization is performed. Should a uterus appear to be too large to interpose, a wedge-shaped resection is performed before the fixation sutures are placed.

The upper flap of parietal peritoneum is now whenever possible sewed to the posterior surface of the uterus, thus excluding the peritoneal cavity and making the operative field extraperitoneal. On quite a few occasions, when the time came to fix the parietal peritoneum to the uterus, I found the latter so thin that successive sutures tore through and the tissue became shredded so that it was impossible to make the attachment. In a few cases the suture placed in the peritoneum for purposes of recognition was cut or tore through the peritoneal flap and could not be found. In these cases, where the wound could not be made extraperitoneal, I observed no difference either in the immediate postoperative course or in the final result.

The bladder is now pushed as far back as possible and held there by a Sims speculum, while the uterus is brought forward just far enough to form a supporting shelf for the bladder and the urethra. The Sims speculum is removed and the uterine cornua and the subpubic tissues are gently scarified with a scalpel blade so as to facilitate cohesion. A suture of chromic catgut is then passed through the scarified area of the corpus on each side and fixed by a deep bite of the needle to the subpubic tissues on the corresponding side of the pubic ramus, with care to keep the bladder up and out of the field so as not to include it in the suture. A suture of similar material is then placed in the upper angle of the vaginal incision in such a way that it includes a good broad bite of the underlying uterus. The bladder is thus sealed off centrally as it was laterally by the subpubic sutures.

Excess vaginal mucosa is resected and the cut surfaces are then apposed from above downward by interrupted sutures of chromic catgut, including a bite of the underlying uterus in the first two or three stitches. A high circular amputation of the cervix is then performed, bleeding is controlled, and the raw surfaces apposed, care being exercised to leave an adequate canal. The canal is then packed with narrow gauze, brought out of the vagina and left loose on the

abdomen to be tied at completion of the operation to the vaginal packing. At times the cervix is so placed or so fixed that its resection would require a good deal of time and probably entail an appreciable loss of blood. In such instances, if it does not appear to be diseased, I prefer not to amputate the cervix. Indeed, some claim that retention of the normal cervix is beneficial as it adds support to the anterior vaginal wall and the bladder.

The operation is not complete and will not yield the best results unless the pelvic floor is repaired. I have included a perineoplasty of the Hegar type in every case in this series. In my hands this type of pelvic floor repair has proved very satisfactory.

I find starch sponge[6] very effective in controlling the venous and capillary bleeding so frequently encountered in separating the bladder and rectum from the vaginal walls. The starch sponge is moistened and placed over the oozing area. Blocks of sponge may be placed against the bladder and rectum and left buried there when the vaginal mucosa is approximated in the usual course of the operation. It need not be removed as it is attacked by enzymes and absorbed by the body fluids.

The vagina is then packed with gauze and a Foley or other form of retention catheter is introduced into the bladder. Instead of using plain or iodoform gauze packing for the vagina I employ starch sponge bandage, which is more hemostatic and its removal is painless.

Indications

The interposition or, as Watkins preferred to call it, the transposition operation is ideally suited for the repair of a large cystocele, especially when it is accompanied by a displacement or prolapse of the uterus of whatever degree in a woman at or after the menopause. In the menstruating woman, it should always be accompanied by tubal sterilization.

Contraindications

The outstanding contraindications are the childbearing age, irregular uterine bleeding, and any other suspicious indications of malignancy. I would also consider a large myoma-bearing uterus a contraindication.

Pregnancy in the woman in whom this operation has been performed is a formidable hazard. While none of my patients became pregnant, I have discussed such a situation with gynecologists in whose practices it has occurred and it makes a hair-raising story. There is almost constant abdominal pain and the urinary tract is dangerously compromised. If the patient goes to term, cesarean section is about the only feasible means of delivery.

Anesthesia

The selection of the anesthetic agent assumes a role of major importance since many of the patients are elderly. Hypertension is a very frequent associated condition as is cardiovascular disease. This series in addition contained several cases of diabetes mellitus and one of bronchiectasis.

The anesthetics used ranged from nitrous oxide, oxygen, and ether administered through an old-fashioned Gwathmey or Bennett machine, to no anesthetic at all.

It might be of interest here to discuss "no anesthetic at all." In talking about the interposition operation with the late George Bonner, he told me that he preferred to have these patients come to him when the prolapse reached their "heels," for then he could operate on them without any anesthetic and thus eliminate the numerous complications one saw in those days following general or inhalation anesthesia.

No anesthesia at all struck me as a very startling statement and I asked him if he meant by that that he employed local instead of inhalation anesthesia. His answer was, "No, I mean none at all, and the reason for this is that the sensory nerve fibers in cases of long-standing procidentia are so attenuated that they fail to transmit pain stimuli."

A short time after this conversation with Bonner, I operated on an old lady suffering from a long-standing procidentia for many years with an associated diabetes mellitus. Apart from a preoperative dose of morphine and scopolamine she received no other type of analgesia or anesthesia. An anesthetist stood by but there being no complaint from the patient his services were limited to observation and an occasional comforting or reassuring remark. Her convalescence was uneventful and the end result was excellent.

In over half of the cases I employed a combination of paracervical anesthesia[7] fortified by rectal instillation of either Avertin or ether in oil. To repair the pelvic floor in patients so anesthetized, I infiltrated the structures with 0.5 per cent procaine solution.

As the anesthetic agents and the skill of the anesthetist improved, I began to eliminate the rectal anesthetics and relied more on the inhalation variety. I continued, however, the use of the paracervical anesthesia, for in this way the consumption of general anesthetics was substantially diminished and I gained the impression that blood loss was materially lessened. I still favor and practice this form of anesthesia. In the very old, I attempt to perform the operation, and usually succeed, by administering a preliminary dose of morphine and scopolamine and following this sedative and analgesic injection by a paracervical injection of 0.5 per cent procaine. This takes care of all the cutting and dissection until the peritoneum is reached. Here I inject a few cubic centimeters into the peritoneum and the structure can then be incised and dilated without producing pain. If pain is complained of while the uterus is being brought forward it can readily be abolished by injecting the broad ligaments which are now under direct vision. Local infiltration of the tissues of the pelvic floor is fully adequate for the repair of these structures. In 1935 I operated on a patient 65 years old under caudal anesthesia and my note records "worked beautifully."

TABLE I

AGE IN YEARS	NO. OF CASES
30-34	12
35-39	18
40-44	15
45-49	10
50-54	10
55-59	16
60-64	10
65-69	6
70-74	2
75-79	1

TABLE II

ADDITIONAL OPERATIONS	NO. OF CASES
Sterilization	39
Myomectomy	10
Partial resection of uterus	2
Advancement of urethra	6
Colpocleisis	1
Repair of anal sphincter	2
Resection of rectal polyp	1
Hemorrhoidectomy	5

This series is composed of one hundred cases. All of them suffered from cystocele, rectocele, and varying degrees of prolapse, the prolapse ranging from first degree to complete procidentia. Fibroids were present in ten patients and six complained of urinary incontinence. The ages ranged from 30 to 79 years and are detailed in Table I.

The cervix was amputated in all but a few cases and the numbers and types of additional operations are detailed in Table II.

Sterilization was performed by cornual resection and no pregnancies occurred in this group.

Comment

It is hard to conceive how any thoughtful person would advocate abolishing an operation which yields so large a percentage of success. In my own series, which to be sure is not very large, I have no knowledge of even one complete failure. There were a trivial number of cases of slight to moderate bulging of the anterior vaginal wall, but no prolapse ever recurred, even in the most marked cases of procidentia. To the best of my knowledge no patient in this series was ever subjected to a subsequent operation to correct the condition for which the interposition operation was performed. I have, however, performed secondary operations for recurrence of prolapse or cystocele after the so-called vaginal plastic and Manchester types of operations.

Rongy[8] reported 501 but performed approximately 1,000 interposition operations on private patients and could find evidence of only six recurrences. That is a remarkable record considering the fact that many of these operations were done before the antibiotic era and at a time when the anesthetics administered were far from ideal and the anesthetists poorly trained by modern standards. His mortality was extremely low, less than 1 per cent. The mortality in my series was nil, and there were no complications of any consequence.

Te Linde[9] states, "This operation has been used extensively in our clinic for uterine prolapse and cystocele, and in most instances the results have been satisfactory."

Satisfactory results can be expected only when patients are individualized and indications and contraindications are conscientiously and intelligently considered. In the early part of this series the operation was performed on women in the childbearing period more often than in the latter years of this report. There being no other contraindications, I would not even now deny this operation to a woman in the latter part of the childbearing period provided she had more than one child and she and her husband granted permission for sterilization. I consider it utterly indefensible to perform this operation in a patient who still menstruates without sterilizing her.

If the operation is avoided in cases where there is a history of a suspicious discharge or of irregular bleeding or assuredly where a preliminary curettage reveals suspicious tissue, subsequent need for diagnostic curettage and radiation or additional surgery will be appreciably diminished. In the same manner, the need for additional procedures would greatly decline if the operation were confined mainly to women beyond the menopause. One of the great drawbacks of this operation in younger women is the difficulty in performing a diagnostic curettage in the horizontal shelflike uterus, should the occasion arise. However, it can be accomplished, especially so if a curette with a flexible shank is employed.

One frequently hears that it is very difficult to remove a uterus after interposition. I recently had occasion to remove such a uterus as did one of the general surgeons in our hospital and neither of us experienced any great difficulty in so doing.

The three best-known procedures which compete with the interposition operation are the Manchester, vaginal hysterectomy, and the Le Fort. No one doubts that the Manchester operation yields very good results. I employ it almost as often, if not more often, than the interposition. As with all operations the Manchester too has its indications and contraindications. I will again quote Te Linde, "It is our opinion that the Manchester operation is a satisfactory procedure 1) where there is a cystocele associated with a prolapse of the first degree, 2) when childbearing need no longer be considered, 3) when the uterus is not in marked retroposition."

Now as to vaginal hysterectomy, very few will at this day argue against removing a diseased or suspicious uterus in a case of prolapse, and yet vaginal hysterectomy is not a logical treatment for an uncomplicated cystocele or uterine prolapse.

The incidence of recurrence after the interposition operation is 3.5 per cent in the Johns Hopkins[9] review. This contrasts with a rate of 30 per cent of unsatisfactory results when vaginal hysterectomy was performed for prolapse. At this point a quotation from Bonney[10] is illuminating, "Finally we would point out that the worst possible course pursuable in a case of prolapse is to remove the uterus. Prolapse is a purely vaginal phenomenon. The uterus not only takes no part in it, but actually by its bulk opposes the descent of the vaginal wall."

While the Le Fort operation gives good results in older and in debilitated patients my own experience leads me to believe that a marked prolapse can be treated with as little shock and with no more blood loss than one encounters in the Le Fort, procedure, and in contradistinction to the Le Fort procedure, the woman is left with a functional vagina. In this age when the span of life has so markedly lengthened a functional vagina is in many instances not merely an academic point.

I have not found the interposition operation per se to be a cure for urinary stress incontinence; on the contrary, a few of my patients developed some degree of incontinence after the operation. Fortunately, the incontinence in these cases was of short duration. Where a patient gives a history of incontinence before operation, I usually combine the interposition operation with a urethral advancement and muscular support of the urethra of the Berkow[11] type. My results in these cases have usually been satisfactory.

I have been applying the interposition technique in vaginal hysterectomy, fixing the round ligaments and the upper portions of the broad ligaments to the tissues behind the pubic rami and to anterior vaginal wall just as one does with the corpus uteri.

The interposition principle has long been employed in cases of descensus following supracervical hysterectomy. In these cases the cervix is utilized in a manner similar to that which one employs with the corpus. My results in this sort of case treated in this way have been extremely satisfactory.

Summary

One hundred cases treated by the interposition operation between the years 1926 and 1951 are reported. The indications are stressed and it is pointed out that if these are intelligently followed excellent results may be expected. A plea is made for the retention of this procedure in the armamentarium of the gynecological surgeon.

Conclusions

The interposition operation has a very definite place in gynecological surgery. Indeed, the operation has no peer in cases of marked cystocele, espe-

cially when the cystocele is accompanied by uterine displacement or any and all degrees of uterine prolapse. It should find its greatest use in women suffering from these conditions, who have passed the childbearing period. When this operation is performed on women who still menstruate, sterilization is essential.

The operation is contraindicated in cases where there is evident or even suspected disease in the uterine corpus.

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1882 Grand Concourse

EFFECTIVE TREATMENT OF DYSMENORRHEA AND MENSTRUAL MOLIMINA BY THE PREOVULATORY ADMINISTRATION OF METHYLTESTOSTERONE OR METHYLANDROSTENEDIOL*

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THE controversial nature of any given subject may be readily surmised when one is faced with a voluminous literature fraught with numerous theories and a variety of different modes of therapy, at times contradictory, one against the other, and based primarily upon empiricism. This is apparent when one considers the subject of functional dysmenorrhea. A review of the literature on dysmenorrhea while lengthy and varied has produced no single thought as to its etiology or the most effective form of therapy for the definitive control of painful menses.[1-3] The totally different methods of treatment based upon equally divergent concepts or theories on the pathogenesis of dysmenorrhea may at times involve the use of agents that are, at best, opposite in action. The numerous reports on the subject attest to the importance of the problem, both physically and economically, and have varied from the unbounded enthusiasm of the ardent therapist to the pessimism of the therapeutic nihilist.[4-10]

The more modern hormonal therapeutic approach to the control of functional dysmenorrhea has been based upon the generally recognized fact that dysmenorrhea is observed only in ovulatory cycles associated with the presence of endogenous progesterone in the patient accompanied by secretory changes in the endometrium.[11-15] Further evidence of the importance of progesterone or the secretory phase in the problem of dysmenorrhea is demonstrated by the effect of exogenous progesterone on menstrual pain. It has been noted that when progesterone is administered to patients without dysmenorrhea prior to menstruation, painful menses may occur in many of these women, or progesterone may actually accentuate dysmenorrhea when given premenstrually to patients exhibiting painful menstruation.[11-13]

With more or less general acceptance of the role of progesterone in dysmenorrhea it was natural, therefore, to utilize hormone therapy directed toward the inhibition of ovulation and thereby prevent the secretory phase or progesterone production by the patient. Estrogens, steroids or those of the stilbene series, have been the preparations of choice for inhibiting ovula-

tion. Numerous reports have appeared demonstrating the effectiveness of preovulatory administration of estrogens in producing anovulatory cycles, and thereby controlling dysmenorrhea.[13, 15-20] However, because of the necessity of suppression of ovulation, disturbance in sequence of menstrual cycles, and refractoriness to therapy in subsequent cycles, the inhibition of ovulation by estrogens for the treatment of dysmenorrhea leaves much to be desired.

The following report is concerned with an investigation of the effect of preovulatory administration of methyltestosterone or methylandrostenediol upon dysmenorrhea. Evidence is offered to show that dysmenorrhea may be effectively controlled by this type of androgen therapy in patients despite the presence of ovulatory cycles associated with secretory changes in the endometrium. Thus, in addition to describing a simple method of controlling functional dysmenorrhea we have also demonstrated that inhibition of ovulation is not necessary for the successful treatment of dysmenorrhea by endocrine therapy. Although the use of methylandrostenediol has not been discussed in the treatment of dysmenorrhea the administration of methyltestosterone prior to ovulation has been presented by Salaber and del Castillo[21] and Davis and Fugo,[22, 23] and more recently by Filler,[24] who adhered to the regimen of Davis and Fugo.

Material

A series of patients primarily with functional dysmenorrhea were treated before and during the ovulatory period with either 10 mg. of methyltestosterone three times a day or 25 mg. of methylandrostenediol twice a day for a period of from six to eight days, starting on the eighth to tenth day of a normal 28 day menstrual cycle. This method differs from those employing premenstrual administration of testosterone by parenteral therapy[25-26] and methyltestosterone[27] or ethinyltestosterone,[28-29] orally, by the time of administration during the menstrual cycle. The therapeutic effectiveness of these steroids when administered premenstrually is not predictable and does not approach the response observed when either methyltestosterone or methylandrostenediol is administered before ovulation. The results were evaluated clinically following the preovulatory administration of the latter two steroids. The effects of these preparations upon body temperature, endometrium, and ensuing pregnancy were also recorded. Endometrial biopsy or the basal body temperature curves were not determined in all patients, but were investigated where feasible. A number of patients whose main presenting complaint was premenstrual tension of a severe degree were also placed on preovulatory doses of methyltestosterone or methylandrostenediol according to the above-described schedule.

Results

The results are summarized in Table I, and the data on individual patients with dysmenorrhea and premenstrual tension receiving methyltestosterone are presented in detail in Tables II and III, respectively. It may be noted that either methyltestosterone or methylandrostenediol were equally and very effective in controlling dysmenorrhea. Excellent or good results were observed in 35 of the 38 patients receiving methyltestosterone and in

8 of the 11 women receiving methylandrostenediol for dysmenorrhea. In two patients with poor results (Table II, Cases 21 and 29) one had a proved case of endometriosis and the other had an associated pelvic inflammatory disease (PID). While these two cases were failures with respect to therapy, they cannot be considered as patients with functional dysmenorrhea. Two patients with suspected, but not surgically proved, endometriosis showed a satisfactory therapeutic effect to methyltestosterone. Perusal of Table II will reveal that 12 patients had received other therapy in the past, by and large, with an unsatisfactory therapeutic effect. Excellent results were noted in 11 of these patients after preovulatory doses of methyltestosterone. It may also be worth while to note at this time that despite the prevalent concept that dysmenorrhea is usually "cured" by pregnancy, 11 of our patients with severe dysmenorrhea had been pregnant and of these nine had children. Dysmenorrhea can be a problem of major concern in women previously pregnant as well as in the nonparous female.

TABLE I. EFFECTIVENESS OF METHYLTESTOSTERONE AND METHYLANDROSTENEDIOL IN DYSMENORRHEA AND PREMENSTRUAL TENSION

PREPARATION	CLINICAL COMPLAINT	NUMBER OF PATIENTS	CLINICAL RESPONSE		
			EXCELLENT	GOOD	POOR
Methyl-testosterone	Functional dysmenorrhea	38	32	3	3
	Premenstrual tension	15	11	2	2
Methyl-androstenediol	Functional dysmenorrhea	11	7	1	3
	Premenstrual tension	5	4	1	0

Note: Eight patients became pregnant while taking methyltestosterone therapy; three of these patients, in addition to dysmenorrhea, also had sterility problems.

No toxic effects due to the medication were noted. There was no evidence of gastrointestinal disturbances so frequently observed when stilbestrol is used to inhibit ovulation. Several patients on methyltestosterone volunteered the information that in addition to relief from dysmenorrhea they also noted an increased feeling of well-being and an increase in libido. None of the patients on methylandrostenediol noted an increase in libido. Two of the patients on methyltestosterone thought there might have been a slight increase in hirsutism while on the androgen. No such untoward reaction was noted with methylandrostenediol.

The doses employed, despite their therapeutic effectiveness, failed to show evidence of inhibition of ovulation. This was manifested by a secretory endometrium on biopsy and ovulatory rise in body temperature in the patients who had taken the androgen therapy. It is also worthy of comment that 8 patients became pregnant during the time that they had been taking the preovulatory methyltestosterone. Three of these patients had had sterility problems in addition to having dysmenorrhea. Pregnancy occurring in sterile patients during methyltestosterone therapy could be ascribed to the relaxing effect methyltestosterone may have on tubal spasm sometimes noted in these patients.[30] The preovulatory administration of androgens while equal to or more effective than estrogen therapy in dysmenorrhea does have the one added advantage in that there is no interference with the ovulatory mechanism. There is also no evidence of alteration in menstrual physiology or regularity. Androgens in the above recommended doses that were employed may be used with impunity for the control of dysmenorrhea in the sterility patient. On

TABLE II. EFFECTIVENESS OF PREOVULATORY ADMINISTRATION OF METHYLTESTOSTERONE
IN THE TREATMENT OF DYSMENORRHEA

PA-TIENT	AGE (YR.)	RACE	GRAV-IDA	PARA	PREVIOUS THERAPY	EFFECTIVE-NESS OF PREVIOUS THERAPY	EFFECTIVENESS OF METHYLTESTOSTERONE
A. L.	24	W	0	0	Dilatation of cervix	Fair	Excellent
					Pavatrine	None	
					Stilbestrol (pre-ovulatory)	Excellent	
M. B.	23	W	0	0	None		Good at first. Poor later (psychoneurotic)
E. B.	20	W	0	0	None		Excellent
R. S.	22	W	i	0	None		Excellent (Pregnancy on therapy)
A. Z.	35	W	ii	ii	Therapy of cervi-citis, erosion	None	Excellent
H. K.	22	W	0	0	None		Excellent (Pregnancy on therapy)
B. P.	18	W	0	0	Testosterone propionate Methyl testosterone Testosterone lin-guets, premen-strually	Not effective	Excellent
I. M.	21	W	0	0	Pavatrine	Fair	Excellent (Pregnancy on therapy)
D. G.	23	W	0	0	Stilbestrol 1 mg. once a day for twenty days	Poor	Excellent
C. O.	37	W	iii	ii	Dilatation of cervix	None	Excellent
J. P.	21	W	0	0	None		Excellent
F. M.	38	W	iii	0	None		Good—Excellent
L. F.	36	W	iii	i	Pranone 10 mg. once a day for 10 days premenstrually	Fair	Excellent
A. P.	26	W	0	0	Aspirin, etc.	None	Excellent
B. H.	24	W	i	i	None		Fair
J. M.	24	W	0	0	None		Excellent (congestion—fi-brosis syndrome)
T. B.	26	W	0	0	None		Excellent with 8 periods; 2 periods with no ther-apy, first fair, second very painful
J. B.	20	W	0	0	Aspirin	Fair	Excellent
					Stilbestrol	Fair	
J. M.	19	W	0	0	None		Excellent (Pregnancy on therapy)
S. K.	22	W	0	0	Stilbestrol	Excellent	Excellent
					Pavatrine	Fair	
					Pranone	Fair	
D. H.	22	W	0	0	None		Poor (endometriosis proved by surgery)
M. M.	35	W	ii	ii	None		Excellent
M. S.	24	W	0	0	None		Excellent
M. W.	26	W	0	0	None		Excellent 2 months, poor 1 month
J. D.	20	N	0	0	None		Excellent
S. S.	26	W	0	0	None		Excellent
R. W.	17	W	0	0	"Needles"	Not good	Excellent
K. P.	30	W	0	0	None		Good (endometriosis pos-sible)
H. R.	37	W	iii	ii	None		Poor (PID)
L. T.	29	W	0	0	None		Excellent (Pregnancy on therapy)
F. J.	28	W	0	0	None		Excellent (endometriosis)
E. N.	25	W	ii	ii	None		Excellent
S. H.	40	W	ii	ii	None		Excellent
L. D.	27	W	0	0	Cauterization of cervix	None	Fair
S. K.	25	W	ii	ii	None		Excellent
I. D.	24	W	0	0	None		Excellent, 3 periods (Pregnancy on therapy)
C. B.	29	W	0	0	None		Excellent (Pregnancy on therapy)
E. D.	28	W	0	0	None		Excellent

TABLE III.   THE EFFECT OF PREOVULATORY ADMINISTRATION OF METHYLTESTOSTERONE ON
PREMENSTRUAL TENSION

NO.	PATIENT	AGE (YEARS)	RACE	GRAVIDA	PARA	RESULTS
1	B. B.	38	W	ii	ii	Excellent
2	R. M.	31	W	i	i	Excellent
3	D. S.	27	W	0	0	Excellent
4	H. P.	32	W	i	i	Not effective in controlling painful engorgement of breasts
5	L.P.	35	W	iv	ii	Good
6	B. M.	33	W	i	i	Excellent
7	G. R.	32	W	0	0	Fair
8	I. K.	18	W	0	0	Excellent
9	D. S.	32	W	ii	ii	Excellent
10	D. T.	38	W	ii	ii	Good—Excellent
11	H. R.	23	W	i	i	Excellent
12	E. V.	41	W	i	i	Excellent
13	R. P.	36	W	iv	ii	Excellent
14	S. N.	21	W	0	0	Excellent (Pregnancy on therapy)
15	E. D.	28	W	0	0	Excellent

the other hand, synthetic or steroid estrogen therapy administered for the purpose of inhibiting ovulation is contraindicated when the problem of sterility is also one of the major considerations. The effect of methyltestosterone on the basal body temperature, dysmenorrhea, endometrium, and ensuing pregnancy is depicted in graphic form in Fig. 1. A rise in the basal body tem-

EFFECT OF PREOVULATORY ADMINISTRATION OF METHYL-TESTOSTERONE OR
METHYL-ANDROSTENEDIOL UPON BODY TEMPERATURE, ENDOMETRIUM,
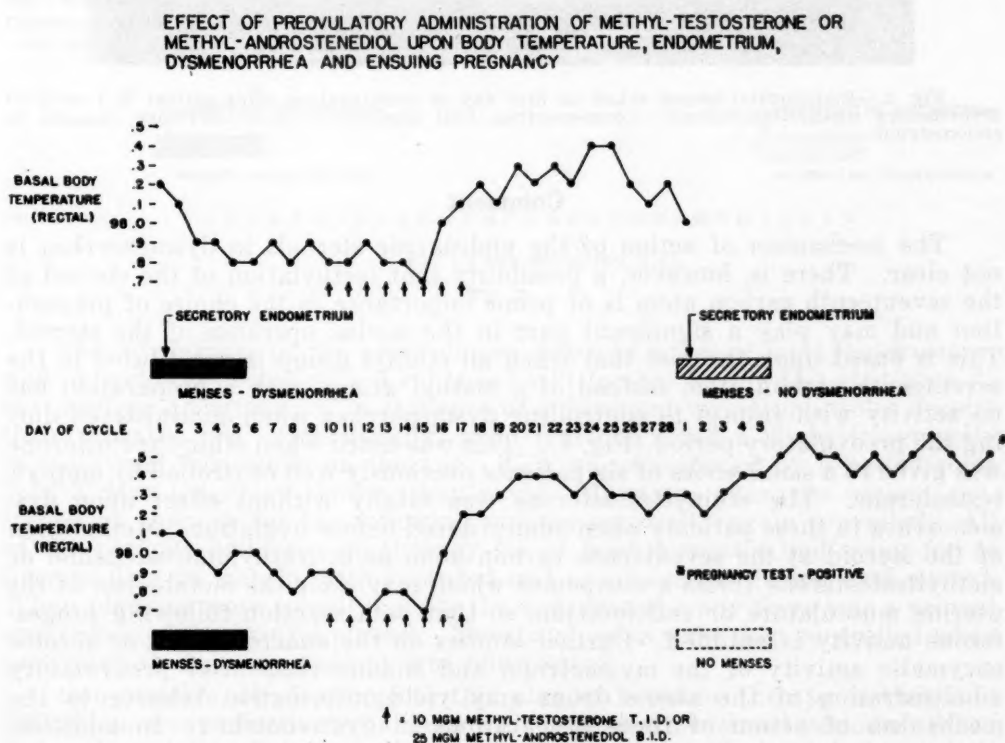DYSMENORRHEA AND ENSUING PREGNANCY

Fig. 1.

perature curve at the time of ovulation together with a secretory endometrium
(Fig. 2) is associated with the absence of dysmenorrhea after androgen ther-
apy.   This is in contrast to Fig. 3 where the response of the patient to pre-
ovulatory administration of estrogen (stilbestrol) is characterized.   While
dysmenorrhea is controlled, ovulation has been suppressed as manifested by a
flat basal body temperature curve and a proliferative endometrium on the
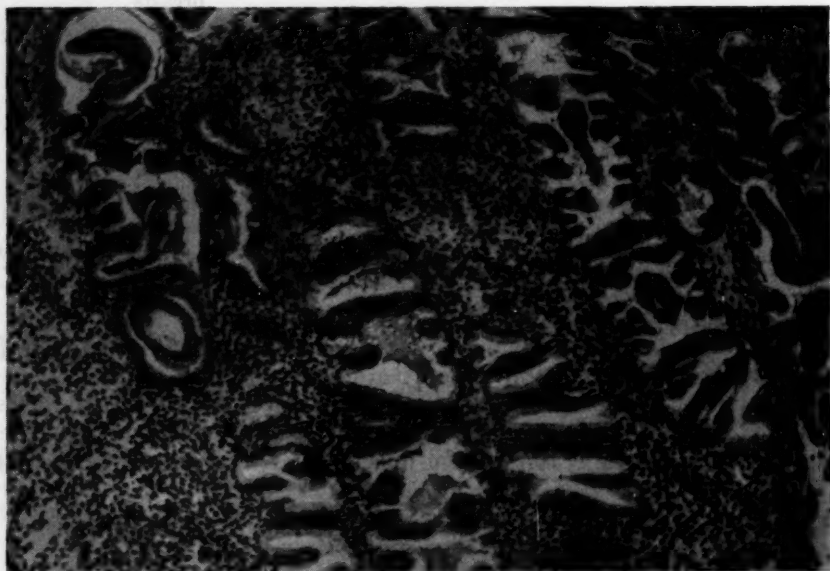first day of menses.

Fig. 2.—Endometrial biopsy taken on first day of menstruation after patient had received
preovulatory methyltestosterone.   Dysmenorrhea well controlled.   Note secretory changes in
endometrium.

Comment

The mechanism of action of the androgenic steroids in dysmenorrhea is
not clear.   There is, however, a possibility that methylation of the steroid at
the seventeenth carbon atom is of prime importance in the choice of prepara-
tion and may play a significant part in the modus operandi of the steroid.
This is based upon the fact that when an ethinyl group is substituted in the
seventeenth carbon atom instead of a methyl group, such a preparation has
no activity with respect to controlling dysmenorrhea when administered dur-
ing the preovulatory period (Fig. 4).   This was noted when ethinyltestosterone
was given to a small series of six patients previously well controlled by methyl-
testosterone.   The ethinyltestosterone was totally without effect upon dys-
menorrhea in these patients when administered before ovulation.   Methylation
of the steroid at the seventeenth carbon atom as in methylandrostenediol or
methyltestosterone forms a compound which may alter the metabolism of the
uterine musculature or endometrium so that pain reaction following proges-
terone activity is nullified.   Further studies on the anaerobic and/or aerobic
enzymatic activity of the myometrium and endometrium after preovulatory
administration of the above drugs may yield information relative to the
mechanism of action of these preparations in dysmenorrhea.   In addition,
uterine pressure studies may reveal changes in the myometrial contraction
pattern after the use of the methylated androgens.

The advantages of the administration of methyltestosterone or methyl-androstenediol in the treatment of dysmenorrhea in addition to their marked effectiveness in controlling pain at the time of menses may be enumerated as follows:

1. Ovulation is not inhibited.
2. The dosage is *usually* not arrhenomimetic.
3. There is no decrease in effectiveness of the preparation after repeated usage.
4. They may be used with impunity in cases of sterility accompanied by dysmenorrhea and in fact may be of advantage due to the effect of the steroid upon relaxation of tubal spasm.

Methylandrostenediol perhaps has the added advantage in that:

1. No arrhenomimetic effects have been noted when administered according to the above plan.
2. It does not increase libido in the dose employed. This may be an important factor when one is called upon to treat young unmarried girls with dysmenorrhea.

EFFECT OF PREOVULATORY ADMINISTRATION OF STILBESTROL UPON BODY TEMPERATURE, ENDOMETRIUM, AND DYSMENORRHEA
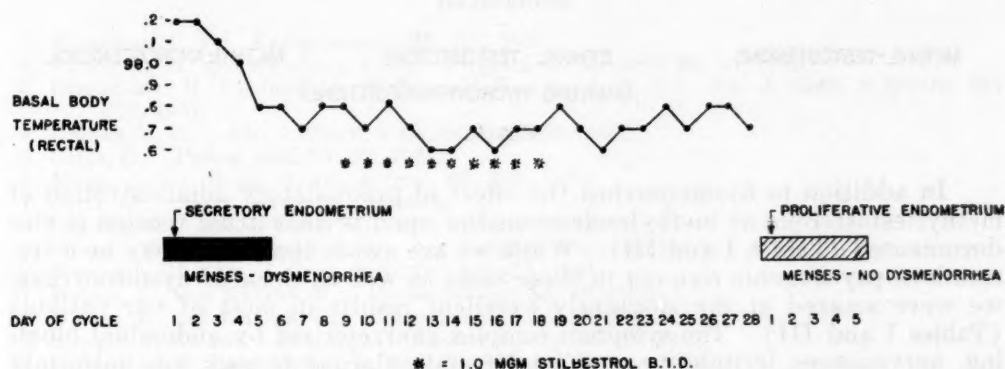

Fig. 3.

The advantages of the preovulatory administration of methylandrostene-diol or methyltestosterone are enhanced still further by the fact that they do not produce an alteration in sequence of subsequent menstrual cycles despite their repeated use. Occasionally, some patients noted a slight irregularity in menstrual flow while on therapy. This was manifested by a period some 2 to 3 days longer or shorter than usual. However, when the patient continued on therapy for the following months regularity again prevailed. All of the patients had been on therapy for at least 4 months and many for as long as 6 to 20 months with repeated and equal success during each period. When placebos were substituted for the androgen therapy there was a prompt recurrence of the painful menses. Menstrual pains were then controlled when preovulatory androgen therapy was reinstituted.

One possible disadvantage to this plan of hormone therapy is that it is difficult to treat effectively patients with irregular menstrual periods. When the medication is administered too early in the cycle prior to ovulation or just at the time of ovulation inconsistent results may be attained. Failures in

therapy may be noted when incorrect timing for the ingestion of the drug occurs. Patients who had been adequately controlled may experience a painful menstrual period if the androgen is administered other than at the prescribed time just before ovulation. The patient with irregular or nonpredictable menstrual cycles, therefore, is not usually a suitable candidate for this therapy. However, any individual with a regular menstrual cycle can be taught to take her medication on a correct schedule for successive menstrual cycles. The patient is guided by the fact that in a 28 day cycle she starts her medication on the 8th to 10th day after her first day of menses. This regimen is changed accordingly for the longer or shorter menstrual cycle.

METHYL-TESTOSTERONE   ETHINYL-TESTOSTERONE   METHYL-ANDROSTENEDIOL
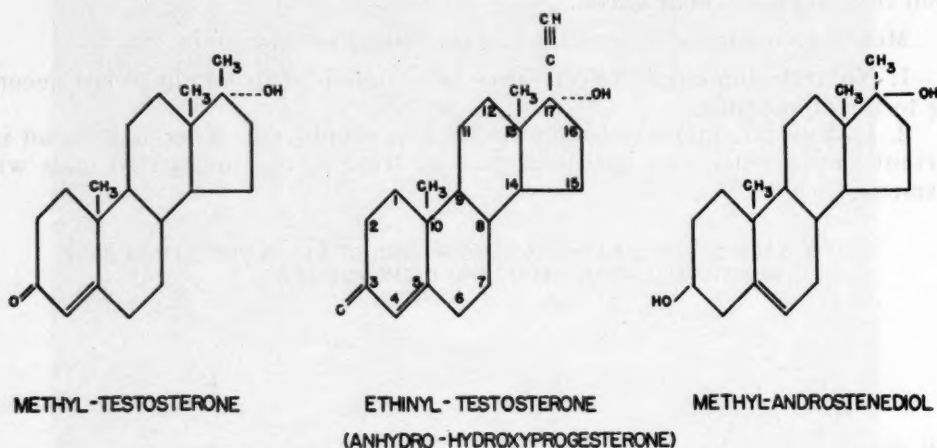(ANHYDRO-HYDROXYPROGESTERONE)

Fig. 4.

In addition to dysmenorrhea the effect of preovulatory administration of methyltestosterone or methylandrostenediol upon premenstrual tension is also documented (Tables I and III). While we are aware that there may be a tremendous psychogenic element in these cases as well as those of dysmenorrhea, we were amazed at the singularly excellent results in most of our patients (Tables I and III). The symptom complex characterized by abdominal bloating, nervousness, irritability, and tender and enlarged breasts was uniformly controlled. Many of these patients who in the past were cognizant of their approaching menstrual cycle by major molimina experienced a menstrual flow without the usually preceding untoward effects after preovulatory therapy with methyltestosterone or methylandrostenediol. The effectiveness of these androgens when given before ovulation against both dysmenorrhea and premenstrual tension permits the use of one therapeutic agent for both conditions. As in the patient with dysmenorrhea alone, administration of methyltestosterone or methylandrostenediol preceding ovulation was effective in controlling premenstrual symptoms in subsequent menstrual periods during the 4 to 12 month period of the study by the repeated administration of the drug.

Summary

Methyltestosterone, 10 mg. three times a day, or methylandrostenediol, 25 mg. twice a day, was administered before ovulation by oral ingestion to a series of patients with dysmenorrhea and premenstrual tension. Either preparation was started 4 to 6 days before the expected day of ovulation and given for 6 to 8 days. Fifty-three patients with dysmenorrhea and/or premenstrual

tension received methyltestosterone while 16 additional patients with comparable symptoms were placed on methylandrostenediol therapy. Both preparations were therapeutically effective and similar in action. The preovulatory use of ethinyltestosterone, on the other hand, did not prove to be effective in controlling dysmenorrhea. The advantage of methyltestosterone or methylandrostenediol over the previous preovulatory use of estrogens in the treatment of dysmenorrhea is that ovulation is not inhibited by the androgens despite the attainment of relief of menstrual pain. This is supported by the fact that a secretory endometrium, an ovulatory rise in body temperature, and several pregnancies were noted after the preovulatory administrations of these androgens in the doses employed. Methylandrostenediol, perhaps, has the added advantage in that arrhenomimetic phenomena following its use in the above dose levels are improbable. Both preparations proved to be effective when used in successive and repeated cycles, and their use was not associated with any disturbance in regularity of subsequent menstrual periods. The possible mechanism involved in the control of dysmenorrhea by the above androgens was not evident. The effectiveness of such therapy, however, indicated that inhibition of ovulation is not necessary in the treatment of dysmenorrhea.

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INTRAUTERINE IMPLANTATION OF OVIDUCTS FOR CORNUAL OCCLUSION BY A REAMER TECHNIQUE*

With a Report of Four Cases

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IT HAS been recognized generally that the results of plastic surgery on bilaterally occluded oviducts for the restoration of patency have been discouraging as far as subsequent pregnancy is concerned. Consequently, patients have not been encouraged to submit to surgery and the number of cases reported has been small.

Holden and Sovak,[1] in 1932, described techniques for the reconstruction of occluded oviducts and reported three cases of cornual occlusion which were treated by implanting the oviducts into the uterine cavity. Patency resulted in two of the three cases. One of the patients with proved patency became pregnant three months postoperatively and was delivered normally at term.

In 1936, Sovak[2] reported a case of ectopic pregnancy in a private patient on whom he had done an implantation operation. At that time he stated that he and Holden had performed a total of fifteen implantation operations on clinic patients, ten of whom they had been able to follow, and six of whom had proved patency. However, pregnancy had resulted in none of these patients except the one reported upon in 1932.

In discussing Sovak's case of ectopic pregnancy, Peightal reported that he had done fifteen implantation operations by the Sovak technique over a period of three years with patency resulting in twelve of them. Unfortunately, none of his patients had become pregnant.

This article is based on four implantation operations done for cornual occlusion by a modified Sovak technique. The postoperative course was afebrile in all of the cases. Antibiotics were not administered in any case.

The operation resulted in proved patency in all four cases. Two of the patients subsequently were delivered of living children (one of them three times). One other patient had a probable but unproved early abortion. The last patient had not conceived eight months postoperatively.

Technique of Implantation

After the abdominal cavity is opened, the site of occlusion is demonstrated by forcing air or normal saline solution from an Asepto syringe into the fimbriated end of the oviduct. The oviduct is severed distal to the occluded area (Fig. 1). The occluded proximal portion is freed from the broad ligament and the patent distal portion is similarly freed for a distance of 1.5 to 2.0 cm. (Fig. 2). A Paton corneal trephine† with a diameter of either 4.5 or 5 mm.

is passed over the occluded stump of the oviduct and, with a rotary motion of the instrument, the interstitial portion is reamed out and the uterine cavity is entered (Fig. 3). The cut end of the patent portion of the oviduct is bi-

Fig. 1.
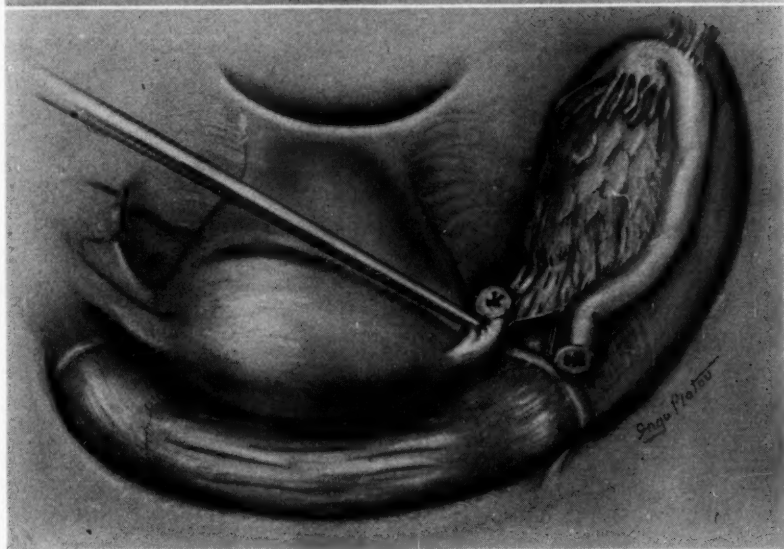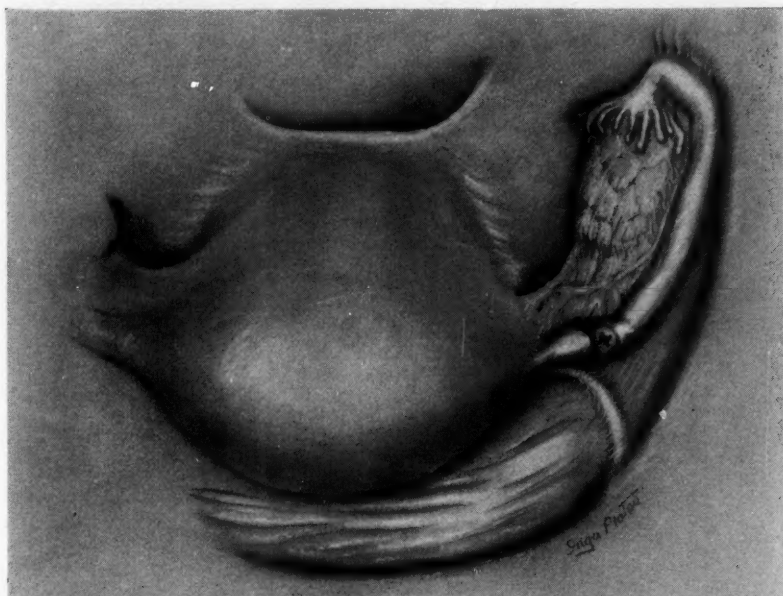
Fig. 2.

Fig. 1.—After the distal limit of stenosis is located by distending the oviduct with air or normal saline solution forced into the fimbriated end through an Asepto syringe, the oviduct is severed distal to the occluded area.

Fig. 2.—The occluded proximal portion of the divided oviduct is cut free from the broad ligament and the patent distal portion is similarly freed for a distance of 1.5 to 2.0 cm.

sected longitudinally with fine scissors for a distance of 1.0 to 1.5 cm. to form anterior and posterior flaps. A No. 00 chromic suture on an atraumatic needle is passed through the end of the anterior flap so that it enters and emerges

on the serosal surface. Both ends of the suture are left long and the needle is cut off. A similar suture is placed in the end of the posterior flap (Fig. 4). The eye of a large Mayo needle is forced through the posterior wall of the

Fig. 3.
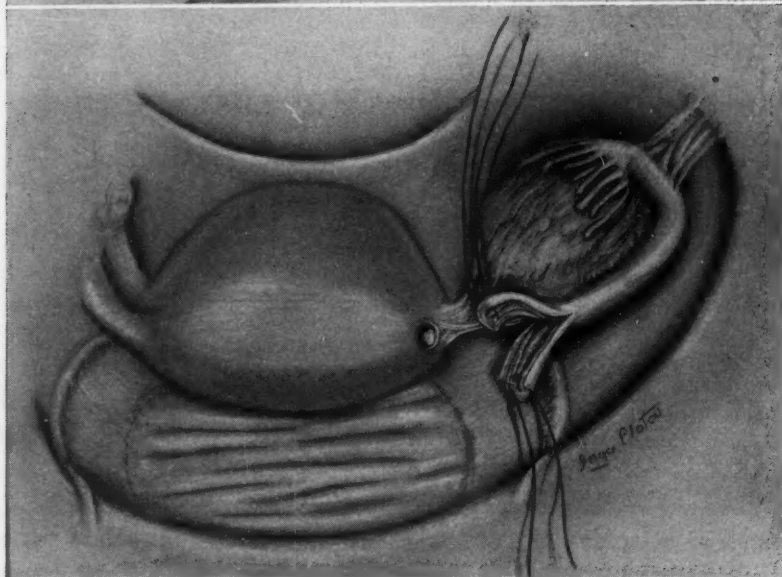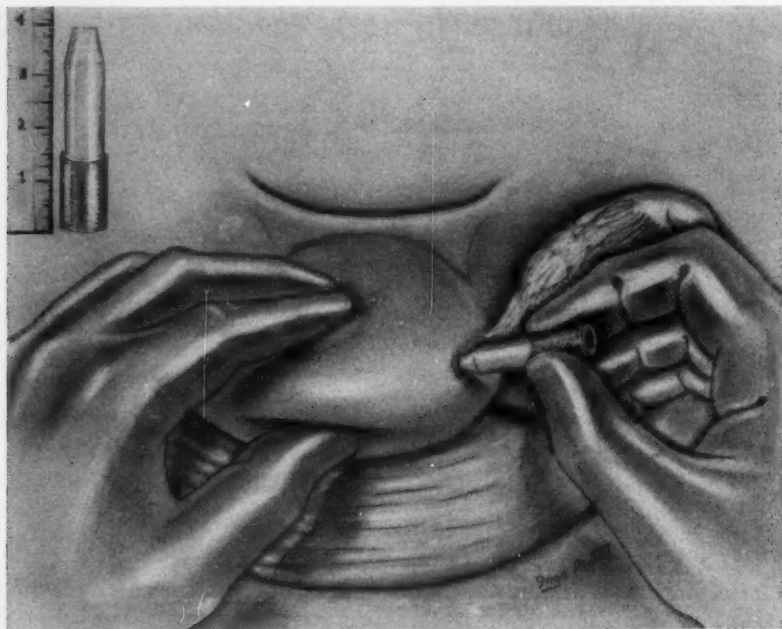
Fig. 4.

Fig. 3.—A corneal trephine (shown in the insert) is passed over the occluded stump of the oviduct and a core of myometrium which includes the interstitial portion of the oviduct is reamed out by forcing the trephine obliquely into the uterus with a rotary movement until it enters the uterine cavity.

Fig. 4.—After the cut end of the distal, patent portion of the oviduct is bisected longitudinally with fine scissors for a distance of 1.0 to 1.5 cm. to form anterior and posterior flaps, a full length No. 00 chromic catgut suture on an atraumatic needle is passed twice through the end of one of the flaps so that it enters and emerges on the serosal surface. The two suture ends are left long and the needle is cut off. A similar suture is placed in the end of the other flap.

Fig. 5.
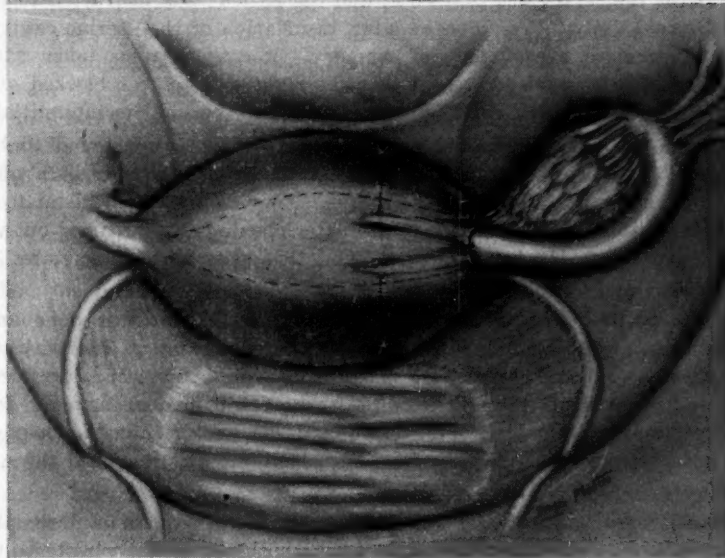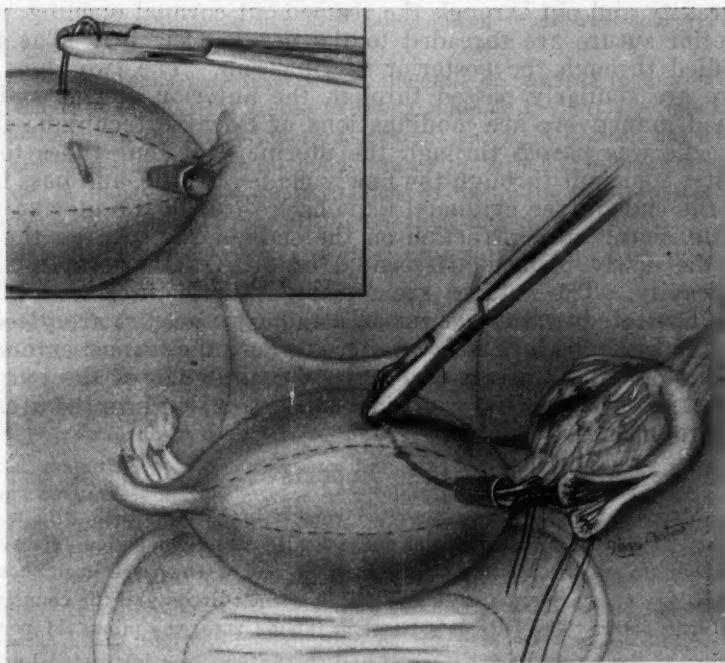
Fig. 6.

Fig. 5.—A large Mayo needle is grasped near its point in a needle holder and the eye of the needle is forced obliquely through the posterior wall of the fundus of the uterus superiorly at a point 1.0 to 1.5 cm. lateral to the midline in such a direction that it enters the uterine cavity (as shown in the insert) and passes out through the newly reamed-out cornual opening. The two long ends of the suture which had been placed in the posterior flap of the oviduct are simultaneously threaded to the needle and are pulled into the uterine cavity and out through the posterior uterine wall. The two ends of the suture which had been placed in the anterior flap of the oviduct are similarly passed through the anterior uterine wall.

Fig. 6.—After gentle, simultaneous traction is made on the ends of both double sutures where they emerge from the surface of the uterus, the oviduct is drawn into the uterine cavity through the reamed-out channels in the cornual area and the suture ends are anchored to the uterus and are tied. Three fine, interrupted catgut sutures are placed through the serosa of the oviduct and the uterus where the former enters the opening in the latter and are tied.

uterine fundus superiorly and 1.0 to 1.5 cm. lateral to the midline, passing into the uterine cavity and out through the reamed-out cornual opening. Both ends of the posterior suture are threaded to the needle (Fig. 5). The two suture ends are pulled through the posterior uterine wall. The two ends of the anterior suture are similarly passed through the anterior uterine wall. (These last described maneuvers are modifications of Sovak's technique in which a Reverdin needle was passed through the uterine wall four times to enter the uterine cavity, come out through the newly made opening, and pass the sutures attached to the ends of the oviductal flaps back through the uterine wall.) By making gentle, simultaneous traction on the ends of the sutures, the oviduct is drawn into the newly reamed-out cornual canal so that the split ends are in the uterine cavity. The sutures are anchored to the uterine wall and tied. Three fine, interrupted catgut sutures on atraumatic needles are placed through the serosa of both the oviduct and the uterus where the former enters the newly created uterine opening and are tied (Fig. 6). Patency of the implanted oviduct is proved by injecting air or normal saline solution into the uterine cavity with an Asepto syringe.

Case Reports

CASE 1.—Mrs. E., 30 years old, presented herself in May of 1943 with a history of a five-year primary sterility. Pelvic examination revealed a second-degree retroversion of the uterus and a moderate erosion of the cervix. Her husband's semen specimen showed excellent motility; morphology of the spermatozoa was within normal limits and the count was 354,000,-000 per cubic centimeter. The patient's basal metabolic rate was minus 11 per cent.

The erosion of the cervix was cauterized and the patient was instructed to take 2 grains of desiccated thyroid daily. Four months later, insufflation of the uterine cavity showed no air through at a pressure of 200 mm. of mercury. Roentgenograms taken after injecting iodized oil into the uterine cavity revealed that the right oviduct was blocked at the cornual end. The left one was visualized for a distance of 1.0 cm. beyond its interstitial portion.

Six months later, a laparotomy was done. The oviducts were found to be "shotty" in appearance and probes passed through their fimbriated ends showed both of them to be stenosed for a distance of 2.5 cm. from the uterus. They were severed distal to the stenosed areas and were implanted into the uterine cavity after openings were reamed out with a 5 mm. trephine. An "angle-worm" reefing of the round ligaments with silk sutures was done to suspend the uterus.

Three weeks postoperatively, intrauterine insufflation of air was done and showed a drop in pressure first at 250 mm., and later at 140 mm. of mercury. The patient complained of slight left shoulder pain after the test. Four months later, a second intrauterine insufflation was done and showed air through at a pressure of 140 mm. of mercury followed by a questionable complaint of shoulder pain. Two and one-half months following the second insufflation, roentgenograms were taken after iodized oil was injected into the uterine cavity and showed no shadows of the oviducts.

Nevertheless, seven months later the patient was curetted for an incomplete abortion of a two and one-half months' gestation, and four months after the curettement she became pregnant for the second time. Twenty-seven months after the implantation operation had been done, in July of 1946, she was delivered by a moderately difficult low forceps extraction of an infant weighing 2,920 grams. At birth, the baby showed signs of cerebral irritation which subsided after a few days.

Fifteen months after delivery, the patient was seen because of a secondary sterility. She was found to have a mild endocervicitis. Flat cauterization of the cervical canal was done. Precoital douches of glucose solution were prescribed. She became pregnant four months later.

Twenty-eight months after her first labor, an elective lower uterine segment cesarean section at thirty-eight weeks' gestation was done because the slight pelvic outlet contraction

which had been demonstrated radiologically during her first pregnancy seemed to have been responsible for cerebral trauma to her first child during labor and delivery. Her second child weighed 3,050 grams at birth.

When the pelvic organs were inspected at the time of cesarean section, a loop of small intestine was found to be adherent to the uterine fundus on the left and was released. Adhesions completely buried the left oviduct and ovary. The right oviduct was adherent to the posterior surface of the uterine fundus but appeared to be patent. There were deep, round depressions 2 cm. in diameter in the cornual regions of the uterus at the sites of the implantations. These depressions admitted the tip of the little finger.

The patient was delivered by lower uterine segment cesarean section in August of 1951 of a third normal infant weighing 3,145 grams.

CASE 2.—Mrs. S., 28 years old, was seen first in April of 1946. She had married at the age of 16, shortly after which a six months' gestation had been terminated by induction of labor. The puerperal period following this labor was reported to have been uncomplicated. Contraceptives were used for eight years until she was divorced in 1942. She remarried in 1945, about a year before she was seen for infertility.

On pelvic examination, the uterus was found to be in third-degree retroversion-flexion and there was a moderately marked erosion of a bilaterally lacerated cervix. Flat cauterization of the cervical erosion was done. Two months later, intrauterine insufflation, after 1/150 grain of atropine sulfate was given subcutaneously, showed no passage of air at a pressure of 240 mm. of mercury. When iodized acacia solution was injected into the uterine cavity, roentgenograms showed that both oviducts were blocked in the cornual regions.

Two months later, bilateral implantation of the oviducts was performed. On opening the abdominal cavity, inspection revealed scarring around the cornual portion of the left oviduct and adhesions of the fimbriated end of the left oviduct to the ovary. The adhesions were separated. The oviducts were severed distal to their occluded areas and a 5 mm. trephine was used to ream out the stenosed interstitial portions. The plug removed on the left side was longer than desirable, measuring 9.5 cm. The plug from the right side was satisfactory, measuring 4 cm. in length. After the implantations were completed, a Baldy-Webster uterine suspension was done.

Three weeks postoperatively, intrauterine insufflation with air indicated patency at a pressure of 80 mm. of mercury. The test was followed by complaint of substernal pain. Six weeks postoperatively, the patient moved to Seattle, Wash., where she reported to Dr. Robert K. Plant for further observation. A letter received from him two months later stated that she was under his care for a pregnancy beginning in October of 1946, three months after the implantation operation had been done. In a later letter, he stated that he had delivered her at term of a 3,035 gram infant and that during labor the cornual areas of the uterus bulged markedly with each contraction until the fetal membranes ruptured, after which the bulging ceased.

This patient, as in the first case, also must have had a secondary sterility, because when she reported back to Dr. Plant a year after delivery, he performed intrauterine insufflation which showed no patency at a pressure of 200 mm. of mercury. Nevertheless, four months later, she had a spontaneous abortion of an eleven weeks' gestation, and two years after that she had another abortion of a nineteen weeks' gestation. Both of these abortions were missed abortions, the fetus in each instance having been dead for a considerable period of time prior to being expelled.

CASE 3.—Mrs. A., 32 years old, was seen first in March of 1947 because of a secondary sterility during three years of a second marriage. She had two children by her first marriage, 10 and 7 years of age. The birth of her first child had been preceded by a spontaneous abortion of an eighteen weeks' gestation. An appendectomy had been performed during her first term pregnancy.

In 1941, a year after her second child was born, a pelvic laparotomy had been performed and a cystic left ovary had been removed, the uterus had been suspended, and the oviducts

had been ligated. At the same time, cauterization of the cervix had been done and the coccyx had been removed. Three years later, a second pelvic laparotomy had been performed by the same surgeon to restore patency and the repair of one oviduct had been attempted.

On pelvic examination, the uterus was found to be anterior in position and somewhat globular in shape. There was a doughy, right adnexal mass about 5 cm. in diameter which was somewhat tender to palpation. Roentgenograms taken after injection of iodized acacia solution into the uterine cavity showed a blocking of both cornual regions.

Because the patient was anxious to have a child by her second husband, it was agreed to attempt intrauterine implantation of the oviducts, although little encouragement of a successful result was given. Seven months after her first examination, a pelvic laparotomy was done. Adhesions of the omentum to the anterior abdominal wall were found and separated. The uterus, which seemed to have been suspended by ventral fixation over an area about 4 cm. in diameter and slightly to the left of the midline, was freed from its attachment to the anterior abdominal wall. Adhesions around the right oviduct which, with part of the omentum, constituted the mass which had been palpated preoperatively, were freed; the blocked cornual portion of the oviduct was excised; and the patent distal portion was implanted into the top of the uterine fundus slightly to the right of the midline. A trephine 4.5 mm. in diameter, instead of 5 mm., was used to ream out a new opening into the uterine cavity because the opening found in the first case at the time of cesarean section had seemed to be larger than necessary.

Three weeks postoperatively, intrauterine insufflation was done and indicated that air passed through the implanted oviduct at a pressure of 80 mm. of mercury. The test was followed by complaint of marked shoulder pain. Basal metabolic rates on this patient had varied from minus 17 to minus 7 per cent and desiccated thyroid in varying doses had been prescribed. In February of 1950, two years and four months postoperatively she had a probable but unproved spontaneous abortion of a two months' gestation. A year later, when last seen, she gave no history of further episodes suggesting pregnancy.

CASE 4.—Mrs. T., 27 years old, reported first in February of 1951 with a history of a two-year primary sterility. Fertility studies carried out at the University of Michigan Medical School fifteen months before had revealed that her husband's semen was normal. Roentgenograms taken after injection of iodized oil into the uterine cavity had shown a blocking at the cornual ends of both oviducts. She gave a history of an appendectomy done in July of 1946 for a colitis of two or three years' duration. A curettement to relieve dysmenorrhea had been done at the same time. Her postoperative course had been afebrile according to a statement by her surgeon. On pelvic examination, the uterus was found to be anterior in position and fairly mobile. There was a slight erosion of the cervix.

Without further study, a pelvic laparotomy was performed. On opening the abdominal cavity, fine adhesions of the fimbriated ends of the left oviduct to the left ovary were found and separated. Adhesions of the fimbriated end of the right oviduct had turned the fimbria in and apparently closed the opening. These adhesions were separated and the fimbriated end was split superiorly and a cuff turned back and sutured to the serosa of the oviduct anteriorly and posteriorly. Injection of normal saline solution into the oviducts demonstrated that both of them were blocked about 2 cm. from the uterus. They were divided distal to the stenosed areas and, as in the third case, a 4.5 mm. trephine was used to make new uterine openings. The distal patent portions then were implanted into the uterine cavity.

Two weeks postoperatively, intrauterine insufflation indicated that air passed into the abdominal cavity at a pressure of 100 mm. of mercury and the test was followed by complaint of moderate right shoulder pain. This patient had not conceived at the time of this report, eight months after the implantations were done.*

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*The patient, however, has been seen since then and has given a history of a clinically confirmed abortion of a ten weeks' gestation occurring a year postoperatively and four months after this paper was presented.

Summary

A method of intrauterine implantation of oviducts for cornual occlusion by a reamer technique, with slight modifications from the method of Holden and Sovak,[1] has been described.

Four cases of bilaterally occluded oviducts treated by this procedure have been reported. Reconstructive surgery in the first case resulted in one abortion followed by the delivery of three living children; in the second case, by delivery of one living child and two subsequent abortions; in the third case, by an unproved spontaneous abortion of a two months' gestation. The fourth case resulted, as did the other three, in patent oviducts, but conception had not occurred eight months postoperatively.

Conclusions

1. The reamer technique of implanting into the uterine cavity the patent portions of oviducts occluded in their cornual portions is worthy of trial for the relief of otherwise absolute sterility.

2. A higher incidence of abortion than occurs normally may be expected following successful implantation operations by the reamer technique.

References

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SAVING THE PREMATURE BABY

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A FEW years ago obstetricians were especially concerned with saving the mothers from hemorrhage, infection, and toxemia, which then took a heavy toll among obstetrical patients. Since the advent of antibiotics, blood banks, and some advancement in the management of the toxemia patient, the concern for the mother is lessened. The obstetrician, therefore, has been enabled to devote more attention to the salvaging of a greater number of the infants, and particularly those who are premature. It is stated that each year 250,000 infants in this country are born prematurely.

According to the standards of the American Academy of Pediatrics, a premature infant is one who weighs 2,500 grams (5½ pounds) or less at birth, whose length is 47 cm. (18½ inches) or less, and whose gestation is 37 weeks or less.

Deaths attributed to premature births account for almost one-half of those in the first month of life, and nearly one-third of all deaths during the first year of life. Because of this appalling fetal loss, a widespread interest has been aroused in how to save the premature infant.

Anderson and co-workers[1] have published several articles on the causes of prematurity. In their review of the literature they found that "prematurity occurs somewhat more often in the births of infants of very young mothers and with first-born children. When the nutrition of mothers is impaired by frequent pregnancies in rapid succession, by insufficient food and rest or by the overstrain of continuous work of a gainful occupation, premature births appear to occur more often than when the mothers are normal."

In their comparison of maternal histories of premature and of full-term infants[2] they state that "in general, it may be said that a history of illness or abnormality of the mother was obtained with greater frequency from women who gave birth to infants of low birth weight and, conversely, that a history of normal pregnancy and spontaneous delivery was obtained with increased frequency from those who bore heavier infants."

"It may be practical," Anderson[3] states, "to establish separate weight standards for the white and Negro races. Five pounds and 8 ounces, or 2,500 Gm., may be considered the lower limit of normal for the white infants and 5 pounds, or 2,300 Gm., as the lower limit of normal for the Negro infants." They also reported[4] that "approximately 80 per cent of the stillborn infants of both races were the offspring of mothers who had had some illness during pregnancy. The majority of stillborn infants were prematurely born (whether or not the mother was in good health during pregnancy). Maternal illness appears to be associated, either directly or indirectly, with about 65 per cent of single live-born premature infants and with 80 per cent of stillborn infants."

It was reported[5] that among the "normal" white mothers premature delivery occurred in 5 per cent, and among those with mild toxemia only the rate was 7 per cent, while in the group with the more severe grades of toxemia it was 17 per cent, and among those with eclampsia it was 38 per cent. When toxemia during pregnancy was accompanied by other illnesses the incidence of premature delivery was even greater. The most significant elevation of rate occurred when bleeding was associated with toxemia.

According to Anderson,[6] "The conditions responsible for uterine bleeding during pregnancy have a more decided influence on the incidence of prematurity than any of the other illnesses commonly associated with pregnancy."

Eastman[7] found that in 60 per cent of all premature births no explanation for the accident can be discovered. In his comments on better prenatal care, he states that there can be "little doubt that poor diet is probably the most common cause of this complication," and that "pills and capsules are no substitutes for the minerals and vitamins found in natural foods."

According to Dana,[8] a certain number of infants who are classified by definition as premature are actually full-term infants, who, for unknown reasons, have failed to attain the weight of 2,500 grams. She reports that the sex ratio of the premature infants was found to be slightly altered, the females predominating. This was also found by Mauzey.[9] Woodbury[10] found a predominance of boys among a large series of premature infants.

Burke, Harding and Stuart[11] found that babies whose mothers' diets have been well supplied with protein have greater birth lengths and weights.

Beck[12] states that there are four important factors that may be responsible for their better results: (1) The physical setup of their nurseries. (2) Excellent cooperation from the Pediatric Department. (3) Discussion of all stillbirths and neonatal deaths at the monthly staff meetings. (4) Reluctance to push sedation beyond the point at which it is safe for the child.

It was found by Beck[12] that anoxia and prematurity were the most common causes of neonatal deaths.

Many premature deliveries, reports Beck,[13] may be prevented and the interruption of pregnancy postponed by adequate care. Delivery by low forceps, preceded by episiotomy, is a desirable method, especially if the second stage tends to be prolonged. Immediate tying of the cord robs the infant of the much-needed bood which he otherwise might obtain from the placenta. Blood in the umbilical cord should be stripped toward the fetus before the umbilical cord is ligated.

Reynolds[14] has shown that during the period of uterine enlargement the uterus is spheroidal. During the period of uterine stretching, it is elongated and cylindrical in shape. The conversion of the uterus from a sphere to a cylinder occurs between the sixth and seventh lunar month of pregnancy. Reynolds also states that "the cardinal fact which seems ripe for exploitation pertains to the relationship between conversion and subsequent fetal maturity at birth."

Burke[15] states that "the incidence of prematurity on the basis of weeks of pregnancy was decidedly reduced in the supplemented diet group."

Carson[16] says, "If they could only give us better specimens to work with."

Toverud[17] says, "The child is nutritionally nine months old at birth," and ". . . prematurity among supervised mothers was less than 50 per cent as frequent as among the non-supervised."

Ebbs[18] states that the incidence of prematurity in women with poor diets was found to be 8 per cent. When milk, cheese, oranges, tomatoes, wheat germ, and vitamin D were added to their diet, the incidence of prematurity was cut down to 2.2 per cent.

Prevention of Prematurity

The incidence of prematurity can be reduced by good prenatal care. A thorough history should be taken when the patient is first seen and a complete physical examination done. The patient should have a blood count, urinalysis, Wassermann test, and Rh determination. Instructions regarding nutrition are necessary. Burke[19] states that "since the amount of protein in the prenatal diet seems to be a significant factor in determining birth length and weight, . . . the diet should be liberally supplied with protein during pregnancy."

If signs of premature labor occur, the patient should be put to bed and the cause of labor ascertained and treated. Sedatives should be administered. Hormones are believed by some to be helpful.

If the attempt to stop the premature labor is unsuccessful, the labor and delivery should be conducted in such a manner as to ensure the infant the best chance of survival. We feel that the management of the premature labor and immediate care of the infant are of utmost importance. There should be no analgesia, or a minimal amount given, and inhalation anesthesia is to be avoided. The preservation of the membranes is necessary for the protection of the baby's head, and a liberal episiotomy should be done to reduce the resistance of the perineal floor. We consider it better to allow the infant to deliver spontaneously, but if the second stage is delayed low forceps should be applied. It is advisable not to sever the cord until pulsations have ceased. According to the work of McCausland, Holmes, and Schumann,[20] stripping the cord, if carefully done, is of definite advantage to the premature infant. In order to clear the infant's respiratory passages, a rubber bulb is usually sufficient. The tracheal catheter should be used with caution. The principal immediate care of the newborn consists of ensuring a clear airway and the administration of oxygen. It is of equal importance that the premature infant be kept warm and be handled as little as possible.

Inasmuch as there are differences of opinion on the management of the premature labor, the following questionnaire was prepared and sent to all the members of the American Board of Obstetrics and Gynecology.

MANAGEMENT OF THE PREMATURE LABOR AND DELIVERY

Analgesia During Labor
Sedatives
    None _____☐
    Minimal amount _____☐
    Regular amount _____☐
Continuous Caudal _____☐

Anesthesia for Delivery
None _____☐
Perineal nerve block _____☐
Low spinal or saddle block _____☐
Caudal _____☐
General _____☐
    Ether _____☐
    Inhalation gases _____☐
    Pentothal Sodium _____☐

Episiotomy
None _____☐   Median _____☐
Small _____☐   Mediolateral _☐
Average ___☐
Liberal ____☐

Delivery
Spontaneous with gentle fundal pressure ____☐
Elective forceps _____☐
Forceps if 2nd stage prolonged _____☐

Management of Cord
1. Clamping and cutting immediately _____☐
2. Waiting until pulsations cease _____☐
3. Gently stripping cord toward infant
   until pulsations cease _____☐
4. Do you consider 2 and/or 3 of benefit
   in combating anemia? _____ Yes ☐ No ☐
5. Do you think stripping the cord causes
   icterus? _____ Yes ☐ No ☐

Clearing of Infant's Respiratory Passages
Bulb syringe _____☐
Soft rubber catheter _____☐
Tracheal catheter _____☐
    If No, do you consider it dangerous?
                      Yes ☐ No ☐

Your suggestions for saving the premature baby:

Of the 2,000 questionnaires sent, answers were received from 1,263. As of special interest the replies from the California physicians were segregated and compiled by themselves; however, they are also included in the group for the entire country. The results of the questionnaire are as follows:

ANALGESIA

	U.S.A.		CALIFORNIA	
	REPLIES	PER CENT	REPLIES	PER CENT
Minimal amount or none	952	75.38	107	69.94
Regular amount	131	10.38	14	9.15
Caudal and combinations	174	13.77	32	20.91
Various combinations	6	.47		
	1,263	100.00	153	100.00

Seventy-five per cent of the physicians throughout the country use minimal or no analgesia, 10 per cent use the regular amount, and 14 per cent use caudal and combinations. California physicians use more caudals. These results reveal the awareness of the obstetricians to the fact that sedation of the mother is deleterious to the premature infant, causing delayed respiration and anoxia with associated hazards.

ANESTHESIA

	U.S.A.		CALIFORNIA	
	REPLIES	PER CENT	REPLIES	PER CENT
Spinal	363	28.74	57	37.25
Caudal	73	5.78	22	14.38
Local	180	14.25	13	8.50
Spinal, caudal, local (varied)	242	19.16	37	24.18
General	205	16.23	14	9.15
Various combinations	200	15.84	10	6.54
	1,263	100.00	153	100.00

As for the U.S.A. group, 29 per cent use spinal anesthesia, 6 per cent use caudal alone, and the remaining 65 per cent use variations of local, spinal, caudal, and general anesthesia. The opinion of the majority is that general anesthesia causes delayed respiration and anoxia in the premature infant.

EPISIOTOMY BY SIZE

	U.S.A.		CALIFORNIA	
	REPLIES	PER CENT	REPLIES	PER CENT
Average	589	46.64	73	47.72
Liberal	343	27.16	35	22.87
Small	110	8.71	14	9.15
Size as indicated	220	17.42	30	19.61
None	1	0.08	1	0.65
	1,263	100.00	153	100.00

It is interesting to note that 74 per cent of the physicians throughout the country use either average or liberal episiotomies. The liberal episiotomy reduces the resistance of the perineal floor against the soft head of the premature infant.

EPISIOTOMY BY SITE

	U.S.A.		CALIFORNIA	
	REPLIES	PER CENT	REPLIES	PER CENT
Mediolateral	505	39.99	44	28.77
Median	406	32.14	70	45.75
Median or mediolateral	351	27.79	38	24.83
None	1	0.08	1	0.65
	1,263	100.00	153	100.00

The mediolateral episiotomy is the type used most throughout the country. It is, however, believed by some, particularly the California group, that the median episiotomy reduces the resistance of the perineal floor more than the mediolateral.

TYPE OF DELIVERY

	U.S.A.		CALIFORNIA	
	REPLIES	PER CENT	REPLIES	PER CENT
Elective forceps	699	55.35	78	50.98
Forceps if second stage delayed	395	31.27	52	33.99
Spontaneous	122	9.66	14	9.15
As indicated	47	3.72	9	5.88
	1,263	100.00	153	100.00

The type of delivery most desirable for the premature infant has aroused a great deal of discussion. Is it better for the premature infant to be born spontaneously or by the aid of low forceps? Elective forceps are used by 55 per cent of the physicians throughout the country, 31 per cent use them when the second stage is delayed, and only 9 per cent advocate the spontaneous delivery. The California physicians are again of the same opinion.

MANAGEMENT OF THE CORD

	U.S.A.		CALIFORNIA	
	REPLIES	PER CENT	REPLIES	PER CENT
Clamping and cutting immediately	382	30.25	21	13.73
Waiting until pulsations cease	527	41.72	44	28.75
Gentle stripping cord toward infant until pulsations cease	247	19.56	63	41.17
Waiting or stripping	67	5.30	16	10.46
As indicated	40	3.17	9	5.89
	1,263	100.00	153	100.00

Thirty per cent clamp and cut the cord immediately, 41 per cent wait until pulsations cease, and only 19 per cent strip the cord. In California 41 per cent strip the cord, probably because of the investigation of McCausland, Holmes, and Schumann.[20] Immediate tying of the cord robs the infant of the much-needed blood which he would otherwise obtain from the placenta.

FURTHER QUESTIONS ON MANAGEMENT OF THE CORD

	U.S.A.		CALIFORNIA	
	REPLIES	PER CENT	REPLIES	PER CENT
Do you think waiting until pulsations cease or stripping the cord combats anemia?				
Yes	662	52.41	114	74.51
No	412	32.62	23	15.03
Noncommittal	189	14.97	16	10.46
	1,263	100.00	153	100.00
Do you think that stripping the cord causes icterus?				
Yes	146	11.56	14	9.15
No	772	61.12	116	75.82
Noncommittal	345	27.32	23	15.03
	1,263	100.00	153	100.00

More than 52 per cent throughout the U.S.A. and 75 per cent of the California physicians believe that waiting until pulsations cease or stripping the cord combats anemia.

About 61 per cent of all physicians in the U.S.A. and 75 per cent of the California physicians believe that stripping the cord does not cause icterus.

CLEARING OF INFANT'S RESPIRATORY PASSAGES

	U. S. A.		CALIFORNIA	
	REPLIES	PER CENT	REPLIES	PER CENT
Soft rubber catheter	339	26.84	10	6.53
Bulb syringe	314	24.86	63	41.17
Tracheal catheter	159	12.59	14	9.15
As indicated	442	35.00	61	39.88
Laryngoscope	8	0.63	5	3.27
Noncommittal	1	0.08		
	1,263	100.00	153	100.00

Thirty-five per cent of the physicians in the U.S.A. use the method indicated for each case in clearing the infant's respiratory passages. One-fourth of the physicians use the soft rubber catheter and another one-fourth use the bulb syringe. The bulb syringe is most popular in California.

FURTHER QUESTION ON CLEARING OF INFANT'S RESPIRATORY PASSAGES

	U.S.A.		CALIFORNIA	
	REPLIES	PER CENT	REPLIES	PER CENT
Do you consider the tracheal catheter dangerous?				
Yes	100	7.92	9	5.88
No	329	26.05	48	31.37
Noncommittal	834	66.03	96	62.75
	1,263	100.00	153	100.00

Very few felt that the tracheal catheter was dangerous, and one-third of the physicians believe that it is of value if used with care. Eight doctors in the country stated that they preferred the laryngoscope.

SUMMARY OF RESULTS OF QUESTIONNAIRE

Analgesia	None or minimal
Anesthesia	Spinal, caudal, or local
Episiotomy	Average or liberal—medial or mediolateral
Delivery	Low forceps preceded by an adequate episiotomy is a desirable method of delivery, especially if the second stage tends to be prolonged
Cord	Wait until pulsations cease, and/or strip the cord
Infant's respiratory passages	Bulb syringe or soft rubber catheter methods mostly used throughout the country

Comment

The purpose of the questionnaire was to obtain the opinion of the certified obstetricians throughout the country on the management of the premature labor and delivery.

One of the major questions was whether it is better for the premature infant to be delivered spontaneously or by elective low forceps.

In 1941 Beck[13] said: "Low forceps preceded by episiotomy is a desirable method of delivery, especially if the second stage tends to be prolonged."

In 1946 Beck[12] said: "Spontaneous vertex delivery accompanied by episiotomy under local anesthesia is the safest method of delivery for premature infants."

In 1946 Dana[8] said: "It was shown that spontaneous or low forceps deliveries were the procedure of choice."

In 1947 Eastman[7] said: "When possible we prefer spontaneous delivery, assisted by fundal pressure, to forceps."

According to the replies received on the questionnaire, 55 per cent of the physicians throughout the country use elective forceps and 31 per cent use forceps if the second stage is delayed.

The small infants usually are delivered easily with gentle fundal pressure after an adequate episiotomy is done. The larger ones do better if delivered by low forceps, particularly if the second stage is delayed. The outcome depends less on the method than on the skill of the physician who does the delivery.

Summary

1. Seven per cent or 250,000 of the infants born each year are born prematurely.

2. Prematurity accounts for one-half of the deaths of infants during the first month of life and one-third of those who die during the first year.

3. One-half of the premature births can be explained; in the other one-half no reason can be found.

4. There is a growing interest among obstetricians, pediatricians, and public health officials in saving the premature baby.

5. The incidence of premature births can be decreased by adequate prenatal care, good nutrition, prompt and proper handling of any complications that occur during pregnancy.

6. If signs of premature labor occur, prescribe (1) bedrest, (2), sedatives, (3) hormones.

7. Management of premature labor and delivery:

    A. Analgesia—none or minimal.

    B. Anesthesia—avoid inhalation anesthesia.

    C. Membranes—preserve the membranes as long as possible to protect the infant's head from pressure against the cervix and perineum.

    D. Episiotomy—liberal to reduce the resistance of the perineal floor.

    E. Delivery—spontaneous or low forceps.

    F. Cord—do not cut until pulsations have ceased.

    G. Clearing of infant's respiratory passages—rubber bulb usually sufficient. Tracheal catheter should be used with caution.

8. Principal immediate care of infant:

    A. A clear airway.

    B. Oxygen.

    C. Warmth.

    D. As little handling as possible.

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401 NORTH BAILEY STREET

TRICHOMONAS VAGINALIS VAGINITIS

Experience With a New Trichomonacide

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THE multiplicity of trichomonacidal preparations available for the treatment of *Trichomonas vaginalis* vaginitis is ample evidence that there is, as yet, no therapeutic procedure that is entirely satisfactory. Many of the therapeutic procedures are time consuming and tedious, and recurrence or reinfection of so-called "cured" cases is more the rule than the exception. The so-called "cured cases" are usually not followed for a long enough period of time; only after three normal menses in which the flagellate cannot be demonstrated should a case be classed as "cured." During pregnancy eradication of the infection is more difficult since foci of infection cannot, at this time, be adequately treated. It has been reported by Whittington[1] that the incidence of *Trichomonas vaginalis* vaginal infestation was 5.3 per cent in a group of 562 women attending a birth-control clinic and 3.4 per cent for 507 women with no gynecologic disorder. It has been generally observed that infestation of the vagina by this flagellate is very frequent in pregnant women in whom thorough treatment, particularly of the cervix, is not possible; it is also frequently present in women complaining of sterility.

The difficulty of therapeutic procedures during pregnancy is well known and therefore a new trichomonacide was used in this Clinic on a group of patients with the hope of finding a procedure which would be innocuous, convenient, and possibly curative.

Purpose of Study

This study was undertaken to investigate a new trichomonacide composed of p-[B is (carboxymethylmercapto) ansino] benzamide in a suppository utilizing a glycerinated gelatin base. Pierce and Morgan[2] investigated this drug in embryonating chicken eggs and found it an effective trichomonacide. In vitro, it is amebacidal to dilution of 1:100,000. Most medication for *Trichomonas vaginalis* vaginitis depends upon a change in pH of the vaginal tract, but this compound seems, apparently, to alter the cell membrane of the flagellate. The preparation has been called by the trade name Arsenamide.†

Toxicity

Arsenic compounds are thought, by some, to be irritants to the vaginal mucosa. The use of tampons treated with 2 per cent buffered solution of Arsenamide inserted into the vaginas of dogs for 24 hours produced only slight redness of the vagina by gross examination. Thus, the preparation in a 2 per cent buffered solution does not seem to irritate the vaginal mucous membrane of dogs.

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The possibility that absorption of arsenic through the vaginal mucosa by the use of this arsenical preparation for a long period of time might result in changes in liver and kidney has been investigated. Arsenamide is definitely absorbed through the mucous membrane of the vagina in the dog, but after repeated administration by this route of a 2 per cent buffered solution for four weeks, the arsenic contents of the liver, spleen, and kidneys of dogs so treated were definitely far below the figure found in fatal cases of human beings poisoned with arsenic.[3]

Method of Study

Subjects for this study were drawn from the Obstetric Clinic of Herman Kiefer Hospital, and, when possible, patients at least three months from term were selected in order that there would be adequate time for evaluation of the trichomonacide. The clinic population is 84 per cent Negro, and the incidence of infestation is approximately 20 per cent.

The diagnosis of *Trichomonas vaginalis* vaginal infestation was made by the use of the hanging-drop technique, using normal saline as the diluent, and all preparations were examined by one individual. Only those patients having two positive laboratory tests for *Trichomonas vaginalis* were considered for the study. A group of 66 patients were catheterized, the urine centrifuged and examined for *Trichomonas vaginalis*, and in 20 cases this organism was found.

As can be expected in clinic practice, subject cooperation was difficult to obtain and thus a complete schedule of weekly examinations was impossible to fulfill. Out of the 94 cases, 75 patients had four or more checkups at weekly intervals and the remainder completed at least two weeks of therapy and were seen on two or more occasions. A postpartum checkup was accomplished in only 25 patients.

All patients were treated on an ambulatory basis and were instructed to insert one Arsenamide suppository high in the vagina every night on retiring.

The subjects studied were divided into three groups depending on the different concentrations of the standard amounts of Arsenamide solution in the vaginal suppositories. A group of 28 pregnant women were treated with suppositories containing a standard amount of a 1 per cent Arsenamide concentrate; these patients will be called Group I. Another group, Group II, consisting of 46 pregnant women, received the same amount of a 0.2 per cent concentrate of the drug per suppository; 20 women in Group III were given suppositories containing the same standard amount of a 0.5 per cent concentrate of Arsenamide.

The patients having bladder infestations of *Trichomonas vaginalis* received, after catheterization, an instillation of 30 c.c. of 1 per cent buffered solution of Arsenamide into the bladder twice a week until two consecutive centrifuged urine specimens were reported negative.

Results

A group of 34 pregnant patients started treatment with vaginal suppositories containing 1 per cent Arsenamide, and of this group only 28 patients returned in one week and thus only these have had adequate follow-up. Of the 28 patients who returned, 21, or 75 per cent, had a negative vaginal smear, which is to say that 25 per cent of the patients continued to harbor *Trichomonas vaginalis*. These 28 patients were continued on therapy and after two weeks of medication all who had had negative smears after one week were still negative and one previously positive smear was now negative, or a total of 22 negative. After four weeks of continuous therapy the results remained the same. Of the seven patients having positive smears after one week of therapy, all except one remained positive after four weeks of continuous therapy with 1 per cent Arsenamide vaginal suppositories; thus there were six failures.

In Group I, six patients stated that the medication "burned" and one stated that soiling of sheets resulted. Accordingly, Arsenamide of 0.2 per cent concentration was placed in vaginal suppositories and Group II, consisting of 46 pregnant patients, was treated with this strength of the preparation.

Following one week of therapy, 32 patients in Group II had negative smears, which constitutes 70 per cent successful results. After two weeks of therapy, 37 patients now had a negative smear, which constitutes a success for the group of 80 per cent. All 46 of the patients in this group were seen after four weeks of therapy with 0.2 per cent Arsenamide and 28 of them still had negative smears; 11 patients who previously had had negative smears now were found to have positive ones. This constitutes a 61 per cent cure after 4 weeks of therapy, provided, of course, that the patients really were inserting a suppository nightly as directed. Thirty-six patients were seen after six weeks of therapy and none of these having previous positive smears were now negative.

Four patients complained of irritation of the vagina during the course of therapy using suppositories containing the 0.2 per cent concentration of the drug.

A third group of 20 pregnant women were then treated for *Trichomonas vaginalis* vaginitis with a 0.5 per cent Arsenamide concentrate vaginal suppository. Twelve patients, or 60 per cent, had negative smears in one week, and after two weeks of therapy 3 patients reverted to a positive smear. After four weeks of therapy only 9 patients, or 45 per cent, had negative smears for *Trichomonas vaginalis*.

One patient complained of vaginal irritation with 0.5 per cent Arsenamide vaginal suppositories.

Table I illustrates the results of the study.

TABLE I. RESULTS FROM NIGHTLY INSERTION OF ARSENAMIDE SUPPOSITORIES FOR TREATMENT OF TRICHOMONAS VAGINALIS VAGINAL INFESTATION

	GROUP I 1% ARSENAMIDE SUPPOSITORIES		GROUP II 0.2% ARSENAMIDE SUPPOSITORIES		GROUP III 0.5% ARSENAMIDE SUPPOSITORIES	
Negative within 1 week	21	75%	32	70%	12	60%
Negative within 2 weeks	22	78%	37	80%	9	45%
Negative within 4 weeks	22	78%	28	61%	9	45%
Failures	6	22%	7	15%	8	40%
Recurrences in 4 weeks	0		11	24%	3	15%
Total number of patients	28		46		20	
Negative post partum (Total 25 cases)	No patients returned		10		3	

Bladder Infestation

Reinfection, either autogenous or from the sexual partner, is so very common that all effort to eradicate the disease may be unsuccessful unless the organism is eradicated from both partners. In women the chief foci for reinfection seem to be Skene's and Bartholin's glands, the endocervical glands, and the urinary tract. In this study catheterization of the bladder was done on 66 patients having *Trichomonas vaginalis* vaginitis and in 20, or 30 per cent, of the patients the flagellate was found. All of these patients were successfully treated by the instillation into the bladder, two or three times weekly, of 30 c.c. of 1 per cent buffered solution of Arsenamide. This drug seems to be very efficacious for eradication of the flagellate from the bladder in women patients.

Summary

1. Arsenamide, an effective trichomonacide in vitro, seems no better clinically than other preparations for the treatment of *Trichomonas vaginalis* vagini-

tis or infestation, during pregnancy. Four weeks' therapy does not increase the cure rate found after one week of treatment.

2. Infestation of the urinary bladder of women with *Trichomonas vaginalis* seems to be successfully eradicated by the instillation of a 1 per cent buffered solution of Arsenamide.

3. Arsenamide seems to cause vaginal irritation in a small number of patients.

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USE OF THE PESSARY*

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FIFTY years ago the pessary was probably used much more than it is today. At that time the literature contained an enormous number of articles dealing with vaginal pessaries.[1] Now such articles are rare.

Why has this change occurred? One reason for the decreased use of the pessary is better selection of cases. Informed doctors today are aware of the indications for a pessary and do not treat asymptomatic retroversions routinely as was the custom in the past.

Even more important is the increased use of the uterine suspension operation in cases formerly treated with the pessary. Fifty years ago, simple, effective, and safe suspension operations had not been devised. It was not until 1900 that Gilliam described his operation for uterine suspension.[3] Webster's suspension operation was published in 1901.[3] Then, too, surgery today does not entail the morbidity and mortality it did in the past. Patients are also aware of this increased safety and are more willing to undergo elective surgery than their grandmothers were.

In most instances, the pessary and the suspension operation are simply two different methods of treating uterine retrodisplacement. Both methods give good results. Unfortunately, physicians too frequently recommend the operative treatment when the simple inexpensive pessary could be used. The indications for the use of the pessary will be discussed first. Later we will summarize the place of the suspension operation.

Uterine retrodisplacement, one of the most frequent indications for the pessary, is present in about 20 per cent of women.[2] Probably not more than 50 per cent of these women have symptoms due to the retroversion. Backache, abdominal pain, dysmenorrhea, menstrual disorders, abortion, infertility, and endometriosis have all been attributed to retrodisplacement. It is possibly true that many of these conditions may be caused by retrodisplacement, but confusion arises because each condition has multiple etiologies.

There is a wide divergence of opinion relative to the amount of backache which may result from retrodisplacement. Undoubtedly displacement and backache are very frequently coincident and yet entirely independent. Postural defects, musculoligamentous derangements, and ruptured intervertebral disc may cause backache in a patient with an incidental retroversion. The presence of retroversion does not mean that it is the cause of the backache. Too often this fact is overlooked.

When retroversion is the cause of backache, the symptoms are usually in the sacral or lumbosacral spine but the character and location of the pain may

vary considerably. The backache is usually dull and increases as the day goes on. If the patient complains of backache before she arises in the morning, and particularly if she gets relief on becoming active, the position of the uterus is probably not responsible for the pain. Such a clinical picture is usually the result of a mild lumbar arthritis. When the diagnosis is in doubt, a therapeutic test with a pessary is invaluable.

Abdominal symptoms of retroversion are "bearing-down pains," a feeling of weight in the pelvis, and a dull ache throughout the pelvis, especially posteriorly. The exact mechanism by which retroversion causes such pain is not clear. Tension on the round and cardinal ligaments and interference with the venous return resulting in broad-ligament varicosities and an enlarged, boggy, tender uterus are possible causes.

In my series of patients with retrodisplacement, 75 per cent of those complaining of backache and pelvic discomfort were relieved by wearing a pessary. Oddly enough some of these patients experienced relief even though the pessary was not effective in keeping the uterus anterior.

Dysmenorrhea is another condition amenable to treatment with the pessary. So-called idiopathic or primary dysmenorrhea is no respecter of uterine position and is found to occur in the anteverted as well as in the retroverted uterus. The stem pessary has been frequently used in the treatment of primary dysmenorrhea on the theory that it promoted free passage of the menstrual discharge. It is not favored today probably because of the infection and uterine perforation which it may produce.

There is no doubt that posterior positions of the uterus may cause dysmenorrhea. It is probable that marked retroflexion of the uterus, resulting in poor drainage of the menstrual flow, is more likely to be a factor than retroversion alone. The menstrual discomfort may take the form of cramps or sacral backache. To evaluate the relation of uterine position to menstrual pain, the uterus should be replaced and a pessary inserted. It has been my experience that 60 per cent of cases of dysmenorrhea and retroversion were relieved with no other treatment than replacing the uterus and inserting a pessary.

Menstrual disturbances may be present with retrodisplacement, but in most instances the position of the uterus has no etiological relationship to the disturbance. For example, amenorrhea, polymenorrhea, hypomenorrhea, and oligomenorrhea of endocrine origin occur with the retroverted as well as the anteverted uterus, and a correction of the uterine malposition will have no curative effect on the menstrual disorder. Likewise, one is never justified in explaining intermenstrual bleeding on the basis of retrodisplacement. When retrodisplacement causes abnormal uterine bleeding it is usually in the form of menorrhagia. In such cases there has usually been retrodisplacement of long standing before abnormal bleeding occurs. An exception is the retrodisplaced puerperal uterus. This enlarged, boggy, bleeding uterus is a wellknown entity. Replacement of the uterus is usually all that is necessary to arrest the bleeding. The mechanism of bleeding in the retroposed uterus is not well understood. It may be due to the passive venous congestion which

causes increased bleeding from the denuded menstrual endometrium. Curtis[4] believes an added factor to be disturbed ovarian function incident to prolapse of the ovaries.

The possibilities of abortion are increased if the pregnant patient has a retroversion. Most writers on the subject agree on this.[6, 7, 8] The boggy, congested endometrium may result in faulty implantation of the pregnancy. Many prominent obstetricians recommend that the pregnant retroverted uterus should be replaced and a pessary inserted. After the third month the uterus rises out of the pelvis and the pessary may then be removed. If replacement is impossible because of adhesions, Curtis advises that the patient stay in bed the first trimester.[5] Repeated abortion occurring in a patient with a retroversion is definitely an indication for insertion of a pessary.

In patients with retroversion permanent sterility is rare, but delayed conception is frequent. Fischmann believes that retroversion is the responsible factor in about 10 per cent of infertility cases.[6] The inaccessibility of the external os to the seminal pool has prompted many physicians to advise patients with retroversion to have coitus in the knee-chest position. Others believe that the edematous endometrium in a retroverted uterus may not afford suitable soil for implantation of the fertilized ovum.[8] With a pessary holding the uterus in an anterior position, both these factors are corrected.

Another indication for pessaries is uterine prolapse. The Hodge and Smith pessaries are effective in minor degrees of prolapse, but if there is an associated cystocele, these pessaries will not stay in position. For such cases, the rubber ring and the Gellhorn pessaries are effective. If there is an associated retroversion along with the cystocele and prolapse, the Gehrung pessary will correct both the prolapse and retroversion. It has an added advantage in that it does not interfere with coitus.

It is also useful to place a pessary in the patient with prolapse who is awaiting surgery. This helps restore tonicity to the pelvic tissues, prevents ulceration and infection of the vaginal mucosa, and permits the vaginal mucosa to regain its normal consistency.

Although there is general agreement that most cases of uterine prolapse are best treated by surgery, there are four classes in which continuation of pessary treatment may be advisable:

1. Patients having only slight or moderate prolapse and who are kept perfectly comfortable by the pessary.
2. Patients with marked prolapse who are poor operative risks and who can be made fairly comfortable with pessary support.
3. Patients with marked prolapse who prefer to get by with the inconvenience and limited relief of pessary treatment rather than to undergo surgery.
4. Younger women with prolapse who desire additional children. The beneficial effects of extensive vaginal repairs in such patients may be nullified by subsequent childbirth.

I have also used pessaries in the absence of any of the usual indications. This has been as a last resort in cases of pelvic pain with obscure or undetermined origin. I was pleasantly surprised when one such patient reported that the pessary had relieved all of her symptoms. This might be explained on the

basis of relieving such things as uterosacral ligament strain, but a much more probable reason is that the symptoms were of psychosomatic origin. A placebo taken orally might have been just as effective.

When the indication for the use of a pessary arises, the advantages of the different types must be considered. We have already discussed those pessaries best suited for treating prolapse. For retrodisplacement, the Smith and Hodge pessaries are the most commonly used. I prefer the Hodge pessary rather than the Smith. In my experience, the Smith type too often slips out from underneath the symphysis. This is probably due to the two lateral bars curving inward where they meet anteriorly. In the Hodge pessary, the lateral bars meet a transverse anterior bar at 90 degree angles. These angles fit snugly in the lateral recesses of the vagina behind the subpubic angle and keep the anterior rim of the pessary from falling down into the introitus. There is a small indentation in the transverse anterior bar to prevent undue pressure on the urethra. The other half of the pessary curves to fit the posterior fornix of the vagina. I find that the Hodge pessary is well adapted to the contours of the vagina and only rarely is it necessary to heat and reshape the pessary to obtain a perfect fit.

When the correct size of the pessary is chosen, it is preferable to use the size that is just a little smaller than a "close fit." One should be able to pass the gloved finger easily between the pessary and the vaginal wall.

After the type and size of pessary have been selected, one should consider how best to elevate the uterus. Bimanual manipulation is often effective. Karnaky[9] reports success in most of his cases by simply inserting the pessary and have the patient stand erect. Another method involves placing the posterior rim of the pessary anterior to the cervix and applying pressure on the pessary until the cervix goes back. This maneuver causes the fundus to come anterior and the posterior rim slips behind the cervix. In difficult cases, a tenaculum may be effective in elevating the uterus. The tenaculum is placed on the cervix and pressure is applied posteriorly until the fundus is elevated. Some writers recommend general anesthesia for the difficult cases.

In my practice, I first try the bimanual method. If this is not successful, I use a maneuver described by Javert.[10] With the patient in the dorsal lithotomy position, the pessary is inserted, the posterior rim placed behind the cervix, if possible. Then the patient is asked to stand up, turn around, and assume the knee-chest position. The labia are separated and the inrush of air into the vagina occurs. Then the fingers are placed on the lateral bars of the pessary, downward pressure is applied, and the patient is asked to cough once or twice. The patient is again placed in the lithotomy position and bimanual examination usually reveals the uterus to be in an anterior position. I prefer this method to the use of the tenaculum, which is often painful and, at least in my experience, not very effective.

If none of these methods is successful in elevating the uterus, I ask the patient to wear the pessary for several weeks and to assume the knee-chest position twice a day. Coughing while in this position produces extreme changes

in intra-abdominal pressure which aid in elevating the uterus. If this method also fails, and all other possible causes of pain have been ruled out, I advise the suspension operation.

If a pessary is properly fitted, the patient is not even conscious of it after the first two or three days. There is no interference with coitus. Continued vaginal pain and dysuria indicate that the pessary is not the proper shape, that it is too large, or that it has slipped out of position.

The vagina is checked at intervals of one to two months at which time the pessary is also cleaned. Irritation of the vaginal mucosa has been rare in my experience and has usually disappeared when a smaller pessary was used. In many instances, the pessary may be removed after four to six months' usage and the uterus will remain in anteflexion.

The contraindication to inserting a pessary is pelvic infection, such as vaginitis, cervicitis, and pelvic inflammatory disease.

In my opinion there are two indications for the suspension operation: (1) retrodisplacement in which the employment of the pessary does not keep the uterus forward sufficiently to relieve the symptoms; and (2) retrodisplacement complicated by other pelvic diseases which require operative treatment. Endometriosis is a good example. A displaced uterus is frequently found in patients with this disease. Those who adhere to Sampson's theory believe that the retroversion may be a cause of endometriosis because of the increased possibility of retrograde menstruation. Even if this theory is not held, it is wise to suspend the retroverted uterus when one is operating on a case of endometriosis. The dense cul-de-sac adhesions preclude the possibility of a pessary holding such a uterus anteriorly.

The uterine suspension operation is a valuable adjunct to the gynecologist's armamentarium. When it is used judiciously there need be no apologies for its use. However, it is unfortunate that only a small proportion of women who have suspension operations are permanently relieved of their symptoms. All too frequently the operation is used in an attempt to relieve symptoms that are not due to the retroversion. If these cases were treated first by a pessary, it would be apparent that the symptoms persist even though the uterus is in an anterior position. The physician is then obligated to search elsewhere for the cause of the symptoms.

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A CORRELATIVE STUDY OF THE BACTERIOLOGICAL AND CLINICAL RESULTS OBSERVED IN THE MANAGEMENT OF COMMON PELVIC INFECTIONS WITH A NEW ORAL PENICILLIN-SULFONAMIDE PREPARATION*

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ONE of the major problems confronting the obstetrician and gynecologist is the correct diagnosis and treatment of pelvic infections. Since the majority of these infections are due to a mixed bacterial population, it is apparent that the use of one antibiotic, such as penicillin, will not provide adequate therapeutic treatment. It would be desirable, therefore, to obtain a chemotherapeutic agent having a wide bacterial spectrum that could be administered orally. The use of such a compound would not only facilitate the ambulatory or home treatment of many of these infections, but would also reduce the nursing care of hospitalized patients.

Recently an oral penicillin-sulfonamide preparation,† containing 100,000 units of potassium penicillin G and 0.166 Gm. each of sulfacetimide, sulfadiazine, and sulfamerazine per tablet, became available for clincal testing. Due to the interest in this problem, it was decided to study this preparation and attempt to evaluate its therapeutic effectiveness in the treatment of the common infections encountered in obstetrical and gynecological hospital wards. An attempt was also made to correlate the clinical and bacteriological results.

Material

Twenty-seven patients, selected at random, ranging from 17 to 45 years of age, admitted to the obstetrical and gynecological services, were chosen for study. The types of clincal infection encountered are listed in Table I.

TABLE I. CLINICAL DIAGNOSIS

CONDITION	NUMBER OF CASES
1. Infected episiotomy	1
2. Threatened abortion	1
3. Incomplete abortion	11
4. Urinary tract infection	2
5. Urinary tract infection complicating pregnancy	2
6. Endometritis	5
7. Acute salpingitis	2
8. Prophylactic	3
	27

On admission, all patient received a complete history and physical examination, in addition to laboratory studies, including cervical and urethral cultures, and urine cultures when indicated. Penicillin disk sensitivity tests[1] were carried out on each of the offending bacteria isolated. Sulfonamide sensitivity tests were not carried out, because of the variation in the results obtained with these compounds, due to their different solubility factors and the neutralization effect of many of the culture media ingredients. As a result there are few practical laboratory procedures for testing susceptibility to the sulfonamides.

Treatment

Treatment of the patients consisted of an initial dose of 6 tablets of the chemotherapeutic preparation, or a total initial dose of 600,000 units of penicillin and 3.0 Gm. of the triple sulfonamide, followed by 2 tablets, 200,000 units of penicillin and 1 Gm. of the triple sulfonamide, every four hours for forty-eight hours. At the end of this time, therapy was reduced to 2 tablets four times a day for the remainder of the treatment period. This dose schedule was based on preliminary studies carried out on normal individuals. The average length of therapy was five days; however, in one case of an infected incomplete abortion, medication was continued for 13 days. Repeated cervical, urethral, and urine cultures were taken throughout the study, and all changes in the bacterial flora and sensitivities were noted. Representative penicillin and sulfonamide blood levels obtained over a six-hour period from five normal women, based on the dosage schedule described above, are shown in Table II. All peni-

TABLE II. BLOOD LEVELS*

TIME (HOURS)	PENICILLIN LEVEL (UNITS)	SULFONAMIDE LEVEL		
		FREE (MG. %)	TOTAL (MG. %)	ACETYLATED (MG. %)
½	0.125	2.6	2.5	----
1	0.5	7.0	7.0	----
1½	0.5	8.8	9.3	0.5
2	0.5	8.9	9.7	0.8
3	0.25	8.4	10.2	1.8
4	0.125	8.8	9.8	1.0
5	0.25	8.7	9.9	1.2
6	0.125	10.6	12.5	1.9
24	0.125	16.3	19.6	3.3

*Average levels obtained from five normal women based on the dosage schedule.

cillin plasma levels were determined by the broth dilution method described by Randall,[2] and the free, total, and acetylated sulfonamide blood levels were estimated by the method described by Bratton and Marshall[3] and read on the Evelyn photoelectric colorimeter. As a result of these preliminary experiments, it was decided that daily determinations of penicillin and sulfonamide blood levels made two hours after the morning medication would give sufficient data for comparative purposes. The dosage schedule was arranged so that all medications were given one hour before meals to prevent excessive penicillin inactivation.

Results

The various types of bacteria cultured from these cases are listed in Table III. It is evident from these results that the staphylococci were the most frequent organisms encountered, followed in order of frequency by the Bacteroides, streptococci, coliform, diptheroides, and Proteus, respectively. These findings are in close agreement with those reported by Hite[4] from her study of infected endometria. Of the 44 cultures isolated, 28 were sensitive to penicillin

and 16 resistant. Infection due to a single type of bacteria was found in only 8 patients, whereas 19 of the patients revealed infections caused by mixed flora.

The penicillin plasma levels determined daily 2 hours after the morning medication ranged from 0.03 to 0.5 unit per milliliter with an average of 0.19 unit per milliliter for all samples tested. In only two instances did plasma levels exceed 0.5 unit per milliliter and in only two individuals were levels less than 0.01 unit per milliliter found. The free sulfonamide blood levels ranged between 5.0 and 22.0 mg. per cent with an average of 12 mg. per cent. The total levels ranged between 1 and 3 mg. per cent higher than those of the free sulfonamide levels. These results are interpreted to indicate merely that adequate therapeutic blood levels are maintained in all patients throughout the treatment period with the exception of two individuals whose penicillin plasma levels were not detectable after the second day.

TABLE III. BACTERIA ISOLATED

BACTERIA	TOTAL NUMBER OF SPECIMENS	PENICILLIN REACTION	
		SENSITIVE	RESISTANT
1. Staphylococci	17	13	4
2. Diptheroides	7	7	
3. Bacteroides	11	11	
4. Coliform bacilli	6		6
5. Proteus sp.	1		1
6. Streptococcus			
Hemolytic	3	2	1
Nonhemolytic	5	3	2
Viridans	1		1
Anaerobic	1		1

Of the 27 patients included in this study, 17 experienced complete clinical cures, and there were three clinical failures. Four patients were dropped from the study due either to their inadvertently receiving other medications, or to their signing their own release from the hospital. Three of the patients received the medication prophylactically; two in conjunction with surgery, and one with a spontaneous unsterile delivery.

TABLE IV. CLINICAL CURES WITH PENICILLIN-RESISTANT CULTURES

DIAGNOSIS	BACTERIA
1. Urinary tract infection	Coliform bacilli
2. Urinary tract infection	Proteus sp.
3. Urinary tract infection during pregnancy	Coliform bacilli
4. Incomplete abortion	Coliform bacilli
5. Incomplete abortion	Staphylococcus

TABLE V. BACTERIAL CHANGE UNDER THERAPY

BACTERIAL CHANGE*	CLINICAL RESULT
1. Bacteroides replaced by a coliform	Failure
2. Sensitive hemolytic streptococcus replaced by a resistant enterococcus	Cure
3. Sensitive diptheroid replaced by a resistant coliform	Cure
4. Sensitive staphylococcus replaced by a sensitive nonhemolytic streptococcus	Cure
5. Sensitive Bacteroides and nonhemolytic streptococcus replaced by a resistant paracolon	Cure
6. Resistant staphylococcus replaced by a resistant coliform	Cure
7. Sensitive staphylococcus and diptheroid replaced by a nonhemolytic streptococcus	Cure
8. Sensitive Bacteroides replaced by a resistant hemolytic enterococcus	Cure

*Resistance and sensitivity refer to penicillin.

Only six of the patients had sterile cultures following therapy. Three of these patients originally had mixed infections, while the remaining three were infected with a single species of bacteria. Cultures obtained from seven patients before treatment were resistant to penicillin, yet five experienced clinical cures (Table IV). There were no changes observed in the bacterial flora of six patients, although 5 of these patients were clinically cured of their infections. There was a complete change in the bacterial flora of 8 patients while under therapy, yet six experienced clinical cures despite these changes. The alterations in the bacterial flora observed in these patients are shown in Table V. It is interesting to note that the coliform and streptococci were the types of organisms found replacing the original flora.

Comment

Today the routine treatment of women with pelvic infections begins with the taking of cervical and urethral cultures, after which the patient is usually started on a combination therapy which consists of penicillin plus some other therapeutic agent. If there has not been a satisfactory clinical response by the time the culture report has been returned, therapy is usually adjusted on the basis of the report and/or the sensitivity tests.

This treatment places great reliance therefore on the culture report and the sensitivity tests. Frequently, however, the clinician finds that there is very little or no correlation between sensitivity tests and clinical response, especially when combined therapy is employed. A more detailed study of the correlation between disk and broth dilution sensitivity tests with the clinical response is indicated.

It will be noted that in this study clinical cures occurred when there were sterile cultures, when there were no detectable changes in the cultures, when there were complete changes in the bacterial flora, and when there were penicillin-resistant bacteria present. In the three clinical failures, one case exhibited no change in the bacterial flora, and two cases exhibited a change in flora. The clinical failure in which no change in bacteria under therapy was exhibited was in a case originally caused by a penicillin-resistant organism. The two other failures in cases in which a change in flora was exhibited during the treatment had originally been caused by penicillin-sensitive organisms with the latent development of penicillin-resistant organisms. (All three failures were subsequently treated with other antibiotics with clinical cures.)

On examination of the data of the six patients who had no change in bacterial cultures while under therapy, one finds that, of the five cures, four patients had intrauterine infections associated with incomplete abortions. These infections were of a mild nature with the temperature never exceeding 100.2° F. Therefore, it is felt that the high clinical cure rate associated with no bacteriological changes in the cultures can be attributed to a mild, well-localized infecfection and good gynecological management rather than to any specific effect exerted by the therapeutic agents which were used.

The bacterial culture changes observed in eight patients under therapy are rather perplexing. There were seven successful cures in this group, despite the bacterial evolution. It is hard to visualize this evolution, but Dienes[5] has observed an evolution in cultures of Bacteroides in the presence of penicillin. Under these conditions he observed that the bacilli swelled into large round forms, were autolyzed, and then a new growth appeared which morphologically belonged to the pleuropneumonia-like organisms. He also noted that the penicillin exerted a similar effect on many gram-negative bacilli.

Fetter[6] reported that combined penicillin and sulfonamide therapy is more efficacious in the management of chronic pyelonephritis and secondary infec-

tions of the genitourinary tract, if gram-negative organisms are present in conjunction with gram-positive cocci. Oard and associates[7] also reported that combinations of sulfathiazole and penicillin were effective for the treatment of gonorrheal urethritis. These clinical observations suggest an additive or synergistic action, resulting from the combination of these agents, and explains, in part, the clinical cures noted in this study despite the presence of penicillin-resistant organisms. Furthermore, according to Demerec,[8] the most effective clinical method of preventing the origin of resistant strains of bacteria is by the use of a mixture of two therapeutic agents that are effective against the same pathogen but differ in their mechanisms of action.

From these observations it appears that uniformly satisfactory results can be obtained in the treatment of the common pelvic infections with a penicillin-triple sulfonamide preparation.

Summary

Twenty-seven patients with common obstetrical and gynecological infections were treated with a new oral penicillin-triple sufonamide preparation Their clinical responses were correlated with pre- and posttreatment bacterial cultures, and to a lesser degree with sensitivity tests.

Combined therapy, such as the preparation used in this study, will invariably give better over-all therapeutic and prophylactic results than will the use of one agent alone. However, there is still no substitute for good obstetrical and surgical technique.

The results emphasize the need for an intensive study of the in vitro in vivo sensitivity correlation.

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THE TREATMENT OF MONILIAL VAGINITIS WITH CAPRYLIC ACID

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THE confusion regarding monilial infections of the vagina rises out of numerous trial-and-error methods of treatment. The percentage of cure is far from satisfactory when one considers the stubborn resistance to therapy that is often encountered, and the frequency of recurrences and exacerbations. Many a patient unfortunate enough to be afflicted makes the rounds of doctors and frequently resolves into an "incurable" left to live with her miserable symptoms. The multiplicity of agents listed for the treatment underlines the therapeutic inadequacy on hand and leaves a gap that is yet to be filled.

Trussell and Johnson[10] reveal a roster of 29 antiseptics and drugs that are fungicidal. Most of these, however, have failed the test of time, probably because they are unable to overcome the associated secondary infection which seems to be a factor in resisting cure.[1] Other pharmaceuticals fail to cure because of their fleeting fungicidal properties.

The advent of modern antibiotic therapy appears to be the most important factor contributing to the ever increasing incidence of this disease. Harris[2] and others[3] point out that mucous membrane manifestations subsequent to aureomycin and chloramphenicol occur in about one-third of the patients and that women are affected more than three times as frequently as men. According to Moore,[9] aureomycin concentration of 0.2 mg. per cubic centimeter culture medium has a stimulating effect on the organism, producing not only large and rapidly multiplying cells but also an increased overproduction of cells as compared to a control (Fig. 1). Keeney[5] showed that penicillin also seems to stimulate the growth of the fungi responsible for the mycotic infections. Concerned over this untoward manifestation, the Council on Pharmacy and Chemistry of the American Medical Association[4] has sounded a note of warning by insisting that all bottles of the orally administered antibiotics carry a statement to the effect that when susceptible bacteria are suppressed by their use yeastlike organisms such as *Candida albicans* may occur. This untoward complication will be attested to by most of the physicians who have administered these preparations.

The need for a satisfactory method of treating vaginitis due to *Candida albicans* has prompted this investigation. It is the purpose of this report to present a promising method of treatment and the results obtained. The formulary embraces the use of sodium and zinc salts of caprylic acid.

Material

The patients selected for this study were obtained from both private and clinic sources, the majority coming from the outpatient gynecologic clinic of the Cook County Hospital.

Any patient who complained of a vaginal discharge was screened for moniliasis by submitting a sample of the vaginal secretion to a fresh hanging-drop examination and inoculation for culture. It became apparent very early in the investigation that there was a marked disparity in the accuracy of the two methods, for at least 30 per cent more positive samples were obtained by the culture method. Since this procedure was far more accurate, it followed that it would be far more critical of a "cure." Hence the wet method was discarded and all subsequent screening and follow-up of treated cases was graded on the basis of the culture result.
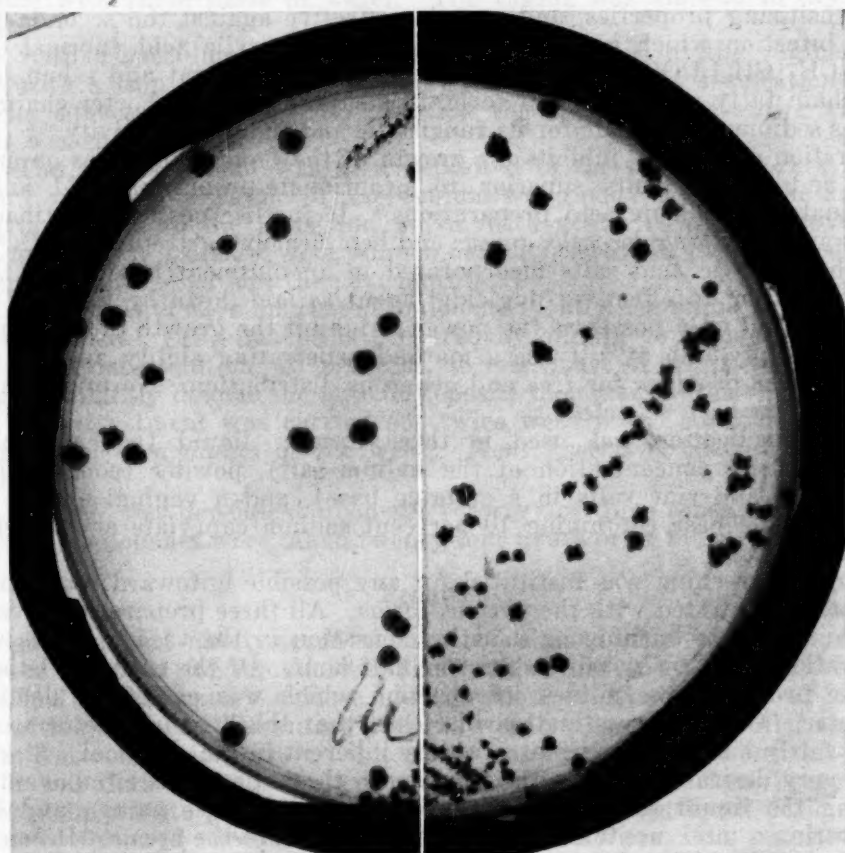
Fig. 1.—Photograph shows comparison between culture growths obtained on plain Sabouraud's agar and modified medium previously incubated with additional antibiotic. On the right, enriched agar shows an abundant fungal growth far exceeding that obtained with the ordinary medium on the left.

A modified Sabouraud's broth was utilized for culture purposes. This medium contained:

Yeast extract	2.5 Gm. per liter
Dextrose	40 Gm. per liter
Sodium chloride	8.5 Gm. per liter

The pH was adjusted to 4.0 and the medium inoculated with 500 units of penicillin and 500 units of neomycin. The vaginal specimen was obtained with a sterile cotton-tipped applicator, placed in a test tube containing the above,

and incubated for 4 days at 37° C. Sabouraud's agar was then streaked with a representative sample of the medium and observed for growth in 24 hours. Microscopic verification of the species was then made.

Treatment was immediately initiated despite the lack of positive diagnosis. This was done to expedite treatment where the culture was positive. Negative cases were not recalled for any therapy.

Caprylic Acid

The fatty acids at present are the most satisfactory agents for treating fungus infections.[5, 6, 7, 8] They combine high fungicidal activity with very low sensitizing properties, and are also effective against the secondary bacterial infection which is invariably present. Caprylic acid (normal octylic acid—$CH_3[CH_2]_6COOH$) is a natural constituent of sweat and sebum. As a long-chain fatty acid in its salt form, it is superior to the shorter chain acids such as sodium proprionate for its fungistatic and fungicidal activity.[5, 6, 7] This preparation completely inhibits the growth of the Candida albicans on an agar plate and gives results superior to proprionate-proprionic acid and undecylenate-undecylenic acid preparations.[6] It further possesses antibacterial action against Staphylococcus aureus and beta hemolytic streptococcus.[5, 6, 7, 8]

The caprylic acid salts incorporated in an ointment base fulfill the requirements for an effective fungicidal agent as laid down by Keeney.[7] This compound not only possesses the power to inhibit the growth of the organism but it actually kills it. It has a marked penetrating ability and its water-miscible base provides for free and generous distribution. No toxic reactions have thus far been reported.

This medication was used in three forms: liquid (aqueous solution of 20 per cent concentration of the sodium salt), powder (combination of the sodium and zinc salts in a suitable base), and a vaginal cream (inert water-miscible base containing 10 per cent sodium caprylate and 5 per cent zinc caprylate).

Initial screening was instituted for any possible untoward reaction, fifty patients being tested with the various forms. All three preparations evoked a mild to moderate burning or smarting sensation in the vagina. This varied in duration from a few minutes to one-half hour. Of the three varieties, the powder provoked the mildest of reaction which was extremely fleeting in character. Careful investigation disclosed that this "pain" factor was due to the fairly marked astringent property inherent in the chemical. Since this was a very desirable feature, the reaction in the patient was circumvented by diluting the liquid form with water (one part to three parts), and by incorporating a mild, nontoxic, mucosal anesthetic into the cream. Because the reaction produced by the powder was of such negligible character, it was not considered necessary to alter the composition.

The choice of a suitable local anesthetic was somewhat complicated by reports from dermatologists that the benzocaine anesthetic commonly used in cough syrups, troches, etc., occasionally produced sensitization when used on the skin and vaginal mucous membranes. This seemed to rule out the use of benzocaine as the local anesthetic agent.

According to the U. S. Dispensatory, twenty-fourth edition, 1948, Saligenin (ortho-hydroxybenzyl alcohol) has a marked anesthetic power in concentrations of 4 per cent to 10 per cent and is practically nontoxic in these concentrations. A vaginal cream containing caprylic acid salts was then prepared in 3 different lots with 2 per cent, 4 per cent, and 10 per cent concentrations of saligenin. These were tried clinically and inadequate analgesic effect noted in the two lower concentrations of saligenin, although 10 per cent proved satisfactory.

Another local anesthetic, propyl para-aminobenzoate, was found to be most effective. With the use of a 4 per cent concentration of propyl para-aminobenzoate no flinching nor complaint of pain or burning upon application of the vaginal cream was noted. Hence all subsequent therapy utilized this type of preparation.

Method of Treatment

All patients were treated similarly.

1. The vagina was thoroughly washed and cleaned with a diluted solution of sodium caprylate. This was done by mixing one part of sodium caprylate with three parts of water. The vagina was allowed to dry thoroughly.

2. With a speculum in place, the cervix and walls of the vagina were coated with a thin layer of the powdered form applied by insufflation using a plastic squeeze container. By rotating the speculum the entire vaginal mucosa was thus covered.

3. The vaginal cream was then deposited in the posterior fornix by an ordinary vaginal applicator. The speculum was removed and a like amount of cream applied to the labia and vulva, with gentle rubbing to cover the entire area. (An ordinary wool tampon can be inserted in place if so desired and removed by the patient the next morning.)

4. The patients were instructed to douche nightly beginning one day after each office visit. (The douche is prepared by adding two tablespoonfuls of sodium caprylate solution, 20 per cent, to one quart of warm water.) Following the nightly douche the patient deposits the cream in the vaginal vault.

5. This treatment was carried out twice weekly and continued at home the remaining five nights of the week. *Menses were no contraindication to therapy.*

A "cure" was dependent upon the recovery of three consecutive negative cultures. No douches were taken twenty-four hours prior to culture.

Results

Eight hundred ninety-seven women complained of a vaginal discharge and were screened for moniliasis. This number provided 124 positive cases established by laboratory culture identification, or 13.8 per cent of the patients with symptoms. Seventeen patients were pregnant. (Monilial vaginitis is quite common in pregnancy. Our series was apparently low for this factor since it was derived from the gynecological clinic only. These pregnancies were seen in private practice.) Treatment was instituted in all patients and completely followed through in 93, including the 17 pregnant patients.

Rapid symptomatic relief followed in all but four women subsequent to the initial treatment. Within 3 to 5 days the vaginal discharge was markedly decreased in amount, assuming a more fluid character, and the pruritus was invariably relieved.

Cultures taken one week after initiation of therapy were negative in 58 patients (62.3 per cent). Two weeks of treatment produced negative cultures in 65 (70 per cent) patients, and following the third week 71 (76.4 per cent) were culture negative. Of the 93 patients, 80 (86.2 per cent) were free of the organism by the end of 5 weeks of treatment as outlined. Thirteen patients failed to show the necessary criteria for cure as previously detailed. Six of these showed one negative culture at some time during the course of their treatment.

These figures can be interpreted from another standpoint. More than one-half became culture negative after 7 days of treatment and maintained this

status through 2 additional weeks of therapy, fulfilling our standard of cure. Seven patients required 2 weeks of treatment before the organism was attenuated, and this finding was maintained for an additional 2 consecutive negative cultures. The small number of patients remaining required at least three weeks of treatment before similar results could be obtained.

All seventeen pregnant patients with moniliasis were cured according to our standard. Six were negative after one week of medication; 12 were negative after two weeks; and the remaining 5 negative after the third week. Three of the total number were beyond 30 weeks' gestation.

These results can be summarized as follows:

Total cases moniliasis		124
Total cases completed treatment		93
Pregnant	17	
Nonpregnant	76	
Total cases with 3 negative cultures		80 (86.2%)
Pregnant	17 (100%)	
Nonpregnant	63 (67.7%)	

The most serious obstacle to a successful outcome in this disease was the history of previous antibiotic therapy. In 34 patients this story was elicited. Antibiotic treatment which antedated our regime by 6 months was not considered sufficient evidence for this factor. However, the length of treatment required to produce a negative culture seemed directly proportional to either the interval between antibiotic and caprylic acid therapy, the intensity of antibiotic therapy, or the antibiotic which produced symptoms and findings of monilial vaginitis.

Of the 13 patents in whom treatment failed, 6 had received a minimum of 4 injections of penicillin, assumed to be a total of at least 1,200,000 units, within 3 months of our treatment; 4 patients noted the symptoms of their vaginitis following aureomycin therapy, necessitating discontinuance of the drug; 3 patients did not receive any antibiotic therapy. In the remaining 21 patients who gave such a history, 7 required 4 weeks of treatment before the first negative culture was obtained, 4 required 3 weeks, 6 were negative after 2 weeks, and 4 were negative subsequent to the first treatment. This last figure represents only 7 per cent of the total number of women negative after one week, while of the number who first became negative beyond the third week, 77 per cent came from those recipients of previous antibiotic therapy. These findings certainly warrant emphasis and further investigation.

Comment

The nuisance factor of vaginal moniliasis has apparently overshadowed any true appraisal of the real pathogenicity of the organism and probably accounts for some of the feeble attempts to evoke a cure. The tremendous variety of agents already in use scores the need for definitive therapy. The modern era of antibiotics has placed an even greater burden on the confused physician and brought a distressing, even though benign, disease on an unsuspecting public. The difficulty of adequate control stems from several factors: (1) The fungal hyphae grow into the epithelial layers and are untouched by most medical agents.[11] (2) The associated secondary bacterial infection is not adequately taken into account as a provocative factor in maintaining the vaginitis. (3) Inadequate evidence of cure (such as negative hanging drop) has relaxed the physician's perseverance in treatment, thus allowing the organism to bloom and give rise to a supposed recurrence or new infection. (4) Previous antibiotic therapy stimulates growth of the organism and apparently increases the resistance to cure.

The fatty acids appear to be the most effective agents as yet uncovered. They possess marked fungistatic and fungicidal properties along with considerable bacteriostatic effect on the usual secondary invaders. The penetrating ability allows for adequate dispersion to all parts of the vaginal tract and contact with the imbedded hyphae is easily obtained. Its action, then, is not dependent on the pH of the vagina.

Caprylic acid in a salt form seems to be the most efficacious of all fatty acids. The rapid clinical and laboratory cure that is obtained is indeed gratifying. The over-all percentage cure of 86 per cent certainly merits further investigation and trial, especially when consideration is given to those patients who have received previous antibiotic therapy. If this were corrected for in this series, the number would rise close to 95 per cent, a false figure of course, but certainly applicable when compared with results of other methods of therapy. We do not feel that this or any other medication will give an everlasting cure. The etiology still remains a mystery. The initial contamination has yet to be scientifically explained, although foci of infection are readily appreciated. In our hands, however, the caprylic acid method stands out as an effective agent in treating the infection present.

Summary and Conclusions

1. Ninety-three cases of vaginal moniliasis proved by culture technique were treated with caprylic acid derivatives. Seventeen patients were pregnant.

2. Using a standardized regime of treatment for all patients, clinical and laboratory "cures" were obtained in 86 per cent within 5 weeks of therapy.

3. The importance of previous antibiotic therapy as a factor contributing to the increasing incidence of vaginal moniliasis and the marked resistance to therapy is presented.

4. Caprylic acid possesses these advantageous properties:

    a. Marked fungistatic and fungicidal action.

    b. Ready penetration of the epithelial layers.

    c. Considerable bacteriostatic effect on *Staphylococcus aureus* and beta hemolytic streptococcus.

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PREGNANCY TOXEMIA WITH BILATERAL RETINAL SEPARATION

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THE occurrence of retinal separation in acute toxemia of pregnancy is a grave complication and one which is sufficiently rare to warrant publication of this report. According to Hallum[4] its incidence is reported to be approximately 2 per cent, although in recent years[5] he appears to be convinced that it occurs much less frequently. Schiotz[6] found 7 instances in 158 cases of eclampsia and threatened pre-eclampsia, while Wagener[7] records having seen only 2 cases at the Mayo Clinic up until 1933. Several other cases[1, 3, 8] complicating pregnancy have been reported by different observers from time to time.

Although the immediate effects of retinal separation impose a serious problem for both the patient and the obstetrician, the prognosis is usually good, spontaneous reattachment of the retina usually taking place within a few weeks following the onset of the acute episode. The detachment is usually bilateral, and may or may not be accompanied by diffuse retinopathy. The origin of the subretinal edema which precedes the detachment has given rise to much speculation. It is debatable whether the edema is to be regarded as part of the general edema present in such cases or whether it is the result of spastic changes in the choroidal arterioles. Crowther and Hamilton[2] suggest that the choriocapillaris may be the source of the edema. The probability of residual permanent vascular disease seems to be distinctly less than in cases of diffuse retinitis of the angiospastic type, commonly seen in chronic hypertensive pregnant patients with superimposed toxemia.

Fortunately, the treatment of these cases is usually simple, consisting essentially of bed rest, cycloplegia with atropine, and binocular dressings. Sedation is continued because of persisting hypertension and proteinuria.

Mrs. G. W., aged 36 years, gravida v, para iv, was a Negro woman with a normal pelvis, negative serology, and negative Rh factor, whose last menstrual period began on Aug. 8, 1950, making her expected date of confinement May 15, 1951. Her menstrual history was normal. Medical and surgical histories were irrelevant. Her father and mother had died of hypertension and ''heart ailment,'' respectively. She had had four normal spontaneous deliveries of viable infants at home, with birth weights ranging from 1,701 to 4,802 grams in 1942, 1945, 1947, and 1949. Her first pregnancy was complicated by elevation of blood pressure, but the remaining pregnancies were essentially uneventful.

Hospital Course.—This patient, who had had no prenatal care during her present pregnancy, was admitted to the hospital on the night of Feb. 19, 1951, in the twenty-eighth week of gestation with the chief complaint of severe frontal headaches, swelling of both ankles and feet of two weeks' duration. She had felt perfectly well until the onset of her present complaints. Total weight gained during her present pregnancy was 19 pounds (8.6 kilograms).

Physical Examination.—Examination revealed a well-developed, fairly well-nourished, middle-aged Negro woman lying in bed in no obvious distress. Her temperature was 98° F., pulse 64, respirations 18, blood pressure 260/140, weight 144 pounds, height 62 inches. The

skin was clear. There was no lymphadenopathy. Extraocular muscles were intact. Bilateral periorbital edema was present. The pupils reacted equally to light and accommodation. Examination of the optic fundi showed subretinal edema bilaterally. Examination of the head, ears, nose, and throat was negative. The thyroid gland was normal. The chest was symmetrical. Lungs were clear to percussion and auscultation. The breasts appeared normal. Heart sounds were normal; no cardiac enlargement or murmurs were apparent. The abdomen was protuberant. The uterine fundus was palpable 20 cm. above the symphysis pubis. The fetus was lying in left occipitoanterior position. Fetal heart tones were not heard. Pelvic examination revealed a parous introitus with good support. There was a moderate amount of discharge in the vagina. The cervix was soft, eroded, and showed a healed stellate laceration. The uterus was anteverted, soft, and enlarged to approximately 28 weeks' gestation, freely mobile, and nontender. Rectal examination was negative. There was one plus edema of the ankles bilaterally. The reflexes were physiological.

Admission laboratory data revealed the following pertinent findings: *Hematology:* hemoglobin 10 Gm. per cent, red blood count 3.94 million per cubic millimeter, white blood count 10,400 per cubic millimeter, polymorphonuclear leucocytes 78 per cent; lymphocytes 21 per cent; eosinophils 1 per cent; monocytes 1 per cent. *Catheterized urinalysis:* specific gravity 10.17, albumin 4 plus; microscopic examination showed 10 to 21 red blood cells, 8 to 10 single leukocytes, occasional fine granular casts, and 1 to 3 coarse granular casts per high-power field.

On Feb. 2, 1951, at 1:00 A.M., the patient had a sudden onset of vaginal bleeding (about 150 c.c.) following which she went into labor spontaneously at 3:00 A.M. and delivered a stillborn fetus weighing 1 pound, 5¼ ounces (595 grams) at 6:18 A.M. The delivery was essentially uneventful and was performed under inhalation anesthesia. Examination of the placenta showed an abruption in one portion of its periphery. Blood loss at the time of delivery was estimated at 200 c.c. Post partum, the patient's blood pressure was 200/125.

Following delivery, the patient began to complain of increasing blurring of vision, scotomas, and severe headaches. Examination of the eyes revealed that the extraocular muscles were normal. The cornea, lens, and media were clear. The right optic fundus showed generalized arteriolospasm. The entire floor of the retina was separated from 4:30 to 8:00 o'clock with ballooning of the detached area to within one papillary diameter of the inferior margin of the disc. There was also an area of separation from 9:30 to 12:00. No tears were seen. Papilledema was present. The left optic fundus showed the entire temporal half of the retina to be detached from 12:00 to 6:00 P.M. Perimacular exudates were seen. Papilledema appeared to be more advanced in the left eye than in the right. A diagnosis of bilateral retinal separation and bilateral papilledema was made and the patient was placed on the following therapeutic regime: (1) complete bed rest, (2) instillation of atropine 1 per cent, 2 drops in each eye, twice daily, and (3) binocular bandages.

Laboratory studies on Feb. 20, 1951, revealed marked impairment of renal function. Blood chemistry examination showed the urea nitrogen 17 mg. per cent, nonprotein nitrogen 26 mg. per cent, uric acid 2.7 mg. per cent, total proteins 3.68 Gm. per cent, albumin 1.90 Gm. per cent, globulin 1.79 Gm. per cent, and albumin-globulin ratio 1.1:1. The heart and the aorta were normal in size and contour. The lung fields were clear. An electrocardiogram showed a left axis deviation, but did not present any specific evidence of myocardial damage.

On Feb. 26, 1951, examination of the optic fundi revealed marked flattening of the area of detachment in both the eyes. There was clearing of disc margins. The patient's blood pressure was 190/110. The hematological findings, urinalysis, and blood chemistry determinations remained essentially unaltered from the previous findings. Thereafter, the patient's blood pressure continued to fall and returned to normal levels (120/80) on Feb. 28, 1951, the tenth postpartum day.

By March 6, 1951, the areas of retinal separation were completely replaced and the discs appeared normal. Two areas of exudate were seen in the right fundus below the disc and one in the superior temporal quadrant of the left optic fundus. She stated that she could see objects better than before. She was allowed to sit on a chair and the eye bandages were replaced by pinhole spectacles.

On March 10, 1951, the twentieth postpartum day, the patient's course was complicated by acute right pyelonephritis which responded satisfactorily to terramycin therapy. Following this she was allowed to get up.

On March 31, 1951, the forty-first postpartum day, a postpartum tubal sterilization by the vaginal route and conization of the cervix were performed under spinal anesthesia. The patient tolerated the operative procedure satisfactorily. Postoperatively, her blood pressure remained around 110/70 until April 8, 1951, the eighth postoperative day when elevation of the blood pressure was noted for the first time to around 170/100. This hypertension was maintained around this level until her discharge on April 12, 1951.

At the time of discharge a complete ophthalmoscopic examination was done. The discs appeared clear at the margins. No exudate was noted. The vision for the right eye was 20/25, and the left 20/25, uncorrected. The blood pressure was 170/110 and weight 116½ pounds. Laboratory data revealed the following findings: *Hematology:* hemoglobin 10.3 Gm. per cent, red blood cells 3.5 million per cubic millimeter, hematocrit, 39 per cent. *Catheterized urinalysis:* specific gravity 10.18, albumin 2 plus, sugar negative. Microscopic: many single leukocytes but no casts. Urine culture negative. *Blood chemistries:* urea nitrogen 16 mg. per cent, nonprotein nitrogen 33 mg. per cent, uric acid 1.85 mg. per cent, total protein 6.72 Gm. per cent, albumin 2.92 Gm. per cent, globulin 3.8 Gm. per cent, albumin-globulin ratio 0.768:1. Renal function studies showed considerable improvement of kidney function.

She was discharged from the hospital on April 12, 1951, the twelfth postoperative day and the fifty-third postpartum day, with instructions to continue restricted activity, sedation, and a high-protein, high-carbohydrate, low-salt diet.

Follow-up.—The patient has now been followed in the Outpatient Clinic at regular intervals for one year. The ophthalmoscopic findings have remained essentially unchanged from those noted at the time of her discharge. Her blood pressure has ranged between 172/108 and 190/130 and her body weight has remained stationary around 116 pounds. Urinalyses of catheterized specimens at various intervals have shown albuminuria (2 plus to 3 plus), a low specific gravity around 10.10, and occasional hyaline casts, a few red blood cells and white blood cells per high-power field. The hematological findings have remained within normal limits. Blood chemistry findings have remained essentially normal except for a persistent elevated plasma globulin with an A:G ratio ranging between 0.58:1 and 0.89:1.

Summary and Conclusions

1. A case of bilateral retinal separation occurring in a pregnant hypertensive patient with superimposed toxemia is described.

2. It would appear that the prognosis for the patient is usually good, and that close cooperation between the obstetrician and the ophthalmologist is essential in the management of such a case.

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SPONTANEOUS HEMATOMA OF THE LIVER IN A WOMAN WITH SEVERE PRE-ECLAMPSIA

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HEMORRHAGE beneath the liver capsule, in pre-eclampsia or eclampsia, extensive enough to cause death, or a large hematoma with survival, is rare. There are five reported cases[1, 3, 4, 5, 6] of rupture of the liver in eclampsia and only one of these patients survived. The liver lesion in toxemia of pregnancy is variable and may be bizarre in its distribution, although when necrosis is present it is most often seen in the right lobe of the liver. The presence of fibrin thrombi in the peripheral hepatic vessels has been regarded by Ingerslev and Teilum[2] as an essential part of the histologic picture. The following case of severe pre-eclampsia, in which there was a spontaneous hematoma of the right lobe of the liver and a successful recovery, is sufficiently rare to warrant reporting.

Case Report.—O. M. W. (HKH No. 95459), a 27-year-old Negro woman, who was a gravida iii, para ii, was delivered in a taxicab at the Herman Kiefer Hospital. There was no history nor evidence of bodily trauma. The patient stated that the last few labor contractions were "violent" in character.

She was first seen in the prenatal clinic May 14, 1951, at which time she stated that her last normal menstrual period had begun on Nov. 11, 1950. The expected date of confinement was calculated to be Aug. 15, 1951. She had been previously delivered at term by outlet forceps of a living infant at this hospital in 1948. A second pregnancy, in 1949, culminated in spontaneous delivery at term of a living infant at home, following an "alleged" normal antepartum course.

The patient's physical examination at the time of her first clinic visit was completely negative. Her blood pressure was 110/70. Her prenatal course was normal until the last visit, two days prior to delivery, at which time the blood pressure was 136/90, and a 5 pound weight gain in two weeks was noted. A 1 plus pretibial edema was present, and a voided urine specimen showed a trace of albumin. The patient was placed on a low-salt reducing diet and was requested to return to the prenatal clinic in one week.

Labor began spontaneously at 2:00 P.M. on July 28 and she was delivered spontaneously three hours later in a taxicab of a living 2,466 gram female infant. The placenta was delivered intact by simple expression. At the time of admission, a few minutes following delivery, the blood pressure was 200/108. There was no clinical evidence of edema. Examination of a catheterized urine specimen revealed a 4 plus albuminuria and rare hyaline casts. Blood studies made at this time gave the following results: nonprotein nitrogen 38 mg. per cent, uric acid 6.8 mg. per cent, total protein 6.1 per cent, hemoglobin 8.5 Gm., and icterus index 3.5 units.

The patient was placed on a severe pre-eclampsia therapeutic regime, consisting of magnesium sulfate intramuscularly, barbiturates orally, bed rest, and the recording of fluid intake and output. Four hours after delivery the patient complained of a severe headache, a sudden, sharp stabbing pain in the right upper quadrant, and associated nausea and vomiting. Her blood pressure was 180/110 at this time, so 10 c.c. of 50 per cent magnesium sulfate was given intramuscularly. Thirty minutes later, or 4½ hours after delivery, she went fairly suddenly into profound shock. Her skin became cold and clammy, the blood pressure went down to 80/50, and the pulse was weak and thready and 120 per minute. Nasal oxygen and

10 per cent intravenous glucose in water were administered. There was no evidence of vaginal bleeding and the uterus was well contracted. At this time an indefinite, tender mass, not previously noted, was palpable in the right upper quadrant two fingerbreadths below the right costal margin. The mass felt as though it was cystic in consistency, and it moved with respiration. The clinical impression was retroperitoneal hematoma from rupture of a perirenal vein, or hematoma of the liver.

The patient recovered rather quickly from the shock status following intravenous hypertonic glucose and inhalation oxygen therapy, and her blood pressure rose to 130/90. She continued to have severe right upper quadrant pain over the palpable mass, however, and it was not relieved following administration of codeine.

Approximately 18 hours after delivery the hemoglobin was found to be 7.5 Gm., or 1 Gm. below the determination made at the time of admission, and, in view of her period of shock and her anemia, 1,000 c.c. of whole citrated blood was administered intravenously.

Following artificial pneumoperitoneum, x-ray studies performed 48 hours after admission revealed a soft tissue mass in the right upper quadrant displacing the small bowel and colon downward and to the left. The cause and nature of this mass could not be determined although it was presumed to be an enlarged liver.

The patient became febrile, developing a temperature of 101.1° F., because of which she was placed on chloramphenicol therapy, being given 2 Gm. daily. Supportive therapy included a high-protein diet and vitamins C and K. She was then transferred to the Surgical Service of the Detroit Receiving Hospital.

Repeated laboratory studies revealed no further change in the patient's hemoglobin. The blood serum test for syphilis was reported to be negative. All catheterized urine specimens continued to show a trace or 1 plus albuminuria. The urine urobilinogen was negative. The prothrombin time was 70 per cent of normal. The bleeding, clotting time, and clot retraction time were normal.

Repeated roentgenological studies of the abdomen showed a large mass, or encapsulated fluid, filling the right upper quadrant and epigastrium, and one observer believed it to have the appearance of a subdiaphragmatic abscess. The liver shadow could not be differentiated from the mass described, and the mass seemed to be increasing slightly in size from day to day.

Twenty-three days after delivery the mass in the right upper quadrant was found to be 5 to 6 cm. below the right costal margin, and it extended posteriorly around to the vertebral column. At this time a needle aspiration at the level of the seventh rib in the posterior axillary line was performed, and 25 c.c. of dark blood was aspirated which did not coagulate. The blood thus obtained was sent to the laboratory and all studies, including bacteriological cultures, were negative. Two days following the posterior approach to the mass an abdominal tap was performed over the area of the mass, and 25 c.c. of dark blood, which did not coagulate, was obtained. During this latter procedure the patient went into shock and was immediately given 1,000 c.c. of whole citrated blood, which brought about immediate recovery.

Laboratory studies at this time, i.e., 25 days after delivery, showed a prothrombin time of 39 per cent of normal. The hemoglobin was 8.5 Gm., even following the transfusion of a total of 2,000 c.c. of whole citrated blood. A catheterized urine specimen showed 2 plus albuminuria and rare hyaline casts, but no white blood cells or red blood cells were present.

Thirty-four days after delivery, on Sept. 9, 1951, an exploratory laparotomy was performed by members of the Surgical Staff, with the expectancy of evacuating the possible subdiaphragmatic hematoma. At the time of surgery a large tumefaction was noted on the anterior and inferior surfaces of the right lobe of the liver. The tumefaction was extremely soft and had the appearance of a hemangioma. Aspiration of the tumor mass for fluid or blood was negative. A biopsy was taken and a considerable hemorrhage from the biopsy site ensued, necessitating suturing and packing with Oxycel to combat the hemorrhage. Immediately following surgery the patient again went into shock,

having a blood pressure of 70/40. The pulse was 140, soft and thready. The rapid transfusion of 1,000 c.c. of whole citrated blood brought the blood pressure to 110/80 and her condition improved.

The pathologic microscopic diagnosis of the biopsy from the tumefaction obtained at laparotomy was "hematoma of the liver."

The postoperative course was somewhat stormy the first 48 hours, with a temperature of 102.4° F., tachycardia, and vomiting. All these symptoms slowly improved under supportive therapy, including 2 Gm. of terramycin daily and intravenous fluids. Icterus appeared three days after laparotomy and the hematoma was palpable 12 cm. below the right costal border. The patient was continued on antibiotic therapy and became ambulatory on the fifth postoperative day. Her gradual improvement continued, and two weeks after laparotomy she was discharged, being continued on oral terramycin therapy. The liver was still palpable 12 cm. below the right costal border the day of discharge.

Laboratory findings at the time of discharge from the hospital showed a negative cephalin flocculation test. The bilirubin was 2.0 mg. per cent. Total protein was 8 Gm. per cent, the albumin being 4.7 and the globulin fraction 3.3 Gm. per cent. The Bromsulphalein test for liver function revealed that 21 per cent of the dye was retained after 45 minutes. The prothrombin time was 100 per cent of normal. A catheterized urine specimen contained only a trace of albumin.

The patient was next seen two weeks after discharge and the liver hematoma in the right upper quadrant was still 12 cm. below the right costal border. The icterus had not diminished. The blood pressure was 120/85. Two days prior to this visit the patient had completed a normal menstrual period which had lasted four days.

One month following discharge from the hospital she was again examined, and the liver was found to be 8 cm. below the right costal border and there was no evidence of icterus. A voided urine specimen was negative. Six weeks after the laparotomy the liver mass was 5 cm. below the right costal margin and the patient was asymptomatic and afebrile.

She was last seen Jan. 15, 1952, at which time the liver was not palpable, and she was 6 to 8 weeks pregnant.

Summary

A case of spontaneous hematoma of the liver occurring in a patient with pre-eclampsia shortly following a precipitous delivery in a taxicab is presented. The possibility of bodily trauma having occurred in the vehicle used for transportation has been considered, but it has been impossible to elicit from the patient any history which might substantiate such a viewpoint. The possibility of rupture of perirenal veins was entertained and this possibility may still remain, but angiograms to prove such a condition were not done because it was thought inadvisable because of the patient's poor condition while in the hospital. The difficulty in establishing a diagnosis has been demonstrated, and many members of the gynecologic, medical, and surgical staffs, who examined this patient, listed several different impressions as to the nature of the disease process. Diagnosis was ultimately made following pathologic study of tissue removed from the enlarged liver at exploratory laparotomy.

Such cases may be fatal if the liver capsule ruptures and permits excessive bleeding from the liver into the peritoneal cavity. The fact that the liver did not rupture in this case may be the important factor in her survival.

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MENINGOCOCCUS MENINGITIS WITH MASSIVE HEMORRHAGE OF THE ADRENALS (WATERHOUSE-FRIDERICHSEN SYNDROME) COMPLICATING PREGNANCY WITH PRE-ECLAMPTIC TOXEMIA

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THE literature on meningococcus meningitis complicating pregnancy is surprisingly scant. Most textbooks on obstetrics fail even to mention it. Those which do pass over the subject very briefly and only in a general way. Thus De Lee and Greenhill[1] merely mention the fact that meningococcus meningitis may occur in pregnancy and may affect the fetus in utero. Adair[2] quotes Greenhill as stating that in 35,000 deliveries not a single case of meningococcus meningitis was encountered. Since meningococcus meningitis is likely to occur in epidemic form, this scarcity of information is remarkable. In a period of more than twenty years at the Cook County Dispensary Hospital, Hoynes[3] was able to collect only three cases of meningococcus meningitis. One patient recovered without a miscarriage; the other two died. Autopsies were not performed.

More recently, Brandeberry and Vergon[4] reported a case of fulminating meningococcus meningitis complicating pregnancy. Despite the fact that the infection in that case was severe, the patient was delivered of a normal baby during the height of the disease, and made a complete recovery. The authors refer to five cases in the foreign literature in all of which the infant survived. They conclude that meningitis has no adverse effect on the course of the pregnancy and that, therefore, the pregnancy should be allowed to run its usual course. This opinion seems to be shared by most other observers. However, the prognosis for the mother is not as good as is that for the offspring. The case to be described below is a case in point and presents features which make it more unique than any previously reported.

Case History.—G. M., aged 34 years, white, a para 0, gravida i, six months pregnant, was admitted to the Prospect Heights Hospital on Dec. 21, 1951, for the treatment of toxemia of pregnancy. For about six weeks prior to admission she had been complaining of headaches, blurred vision, and swelling of the legs. During this period her blood pressure had been steadily rising, accompanied by a persistent and marked albuminuria. About two weeks prior to hospitalization she had had an upper respiratory infection from which she recovered following penicillin therapy. Her past history is irrelevant.

Physical examination on admission to the hospital showed a normal temperature, pulse 80, respirations 20, and a blood pressure of 138/110 which later rose to 180/130. There were no casts found in the urine and the specific gravity ranged from 1.012 to 1.024. The blood urea nitrogen levels ranged between 9.3 mg. per cent and 15 mg. per cent, with a creatinine of 1 mg. per cent. The serum protein was 5.2 Gm. per cent, of which 3.19 Gm. were albumin and 2.01 Gm. were globulin (ratio 1.5:1). The total chloride was 600 mg. per cent.

The patient was treated with intravenous glucose (5 per cent), phlebotomy, and blood transfusion. The toxemia progressed and it was decided to terminate the pregnancy. On December 27, following prophylactic administration of penicillin, the membranes were ruptured and a Voorhees bag was inserted under saddle anesthesia. About 12 hours later she expelled the bag and labor began to progress slowly and intermittently thereafter, until

December 29, at 5:35 P.M., when she precipitated a stillborn, macerated, female fetus. The placenta was delivered spontaneously and appeared intact. There was only a moderate amount of blood lost and the uterine fundus remained firmly contracted.

About two hours post partum, the patient developed deep shock which was dramatically combated by transfusion of 1,000 c.c. of blood. The temperature, which until the day of delivery had remained normal, now rose to 102.5° F., then declined to 99° the following morning, only to rise again to 101° that night. Mental changes, consisting mainly of delusions of persecution, were noted soon after delivery and persisted until the following morning, when she told the nurse who attended to her last at 8:45 A.M., that she feared she was going to be poisoned and that she did not expect to live. Two hours later she was found dead. The cause of her death was not apparent clinically and occurred as a complete surprise.
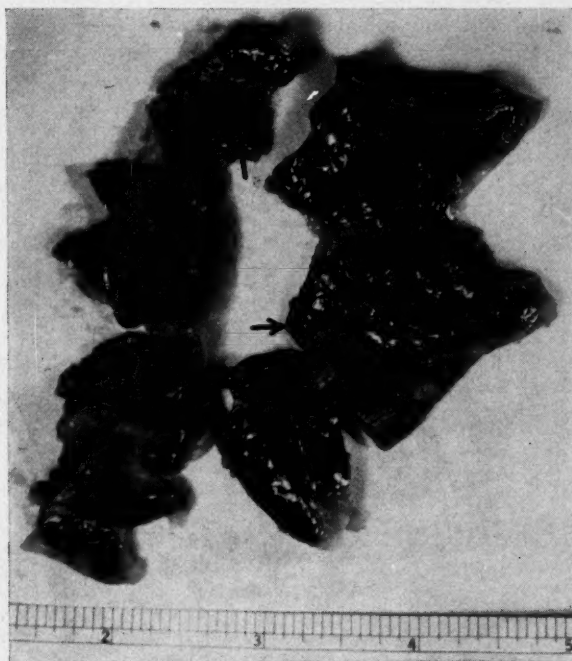

Fig. 1.—Gross specimen of adrenals showing the massive hemorrhage (arrows) destroying cortex and medulla of the organs.

Postmortem Protocol No. 532.. (Summary of positive findings).—The head showed an unusual degree of cyanosis. There was about 300 c.c. of clear yellow fluid in the right pleural cavity. The heart weighed 250 Gm. and the cardiovascular system was essentially normal. The lungs showed fibrous, apical, scars and fibrin thrombi in some of the smaller branches of the pulmonary arteries, with adjacent small hemorrhagic infarcts. One section showed an osseous embolus in an interalveolar capillary, being engulfed by a macrophage. The gastro-intestinal system was essentially normal except for a hugely dilated stomach, filled with undigested food, and a hemorrhagic epiploon in the mesentery. The pancreas weighed 100 grams and was normal. The liver weighed 1,725 grams and showed mid-zonal and periportal foci of necrosis with acute inflammatory infiltrate. The vessels within these areas showed fibrinoid degeneration. The kidneys weighed 240 grams each and showed marked cloudy swelling of the tubules, some with hyaline casts, occasional foci of acute inflammatory infiltrate in the interstitial tissue, and marked glomerular changes, consisting of fibrinoid necrosis of afferent arterioles with degeneration of glomerular capillaries in some and occlusion of capillaries by fibrin thrombi in others. Many glomeruli were almost devoid of blood and the endothelial cells of their capillaries were markedly swollen. The uterus measured 22 cm. in greatest dimension. The myometrium was soft and the cavity was filled with blood clot and some

retained placental tissue. The spleen weighed 160 grams and showed perifollicular foci of fibrinoid necrosis. There was also a marked polynuclear and plasma-cell infiltration in the parenchyma. The adrenal glands weighed 30 grams, appeared blue black in color, and were almost completely destroyed by massive hemorrhage. In the fascicular zone of the cortex, radial rows of bacterial colonies of cocci were demonstrable. Scarcely any medullary tissue remained. The pituitary gland was moderately enlarged by eosinophilic cell hyperplasia. The sternal marrow showed considerable hyperplasia with a marked left shift of granulocytes. The brain, which weighed 1,465 grams, and the meninges showed no changes grossly, but smears of the pial surface of cortex and base showed a pure culture of gram-negative diplococci which were culturally Neisserian. Similar organisms were found in the spinal fluid removed from the cisterna magna, although it appeared to be clear grossly and showed a minimal increase in the cell count (82 per cubic millimeter). However, microscopic sections of the meninges of the brain and spinal cord showed extensive purulent infiltration of all layers.
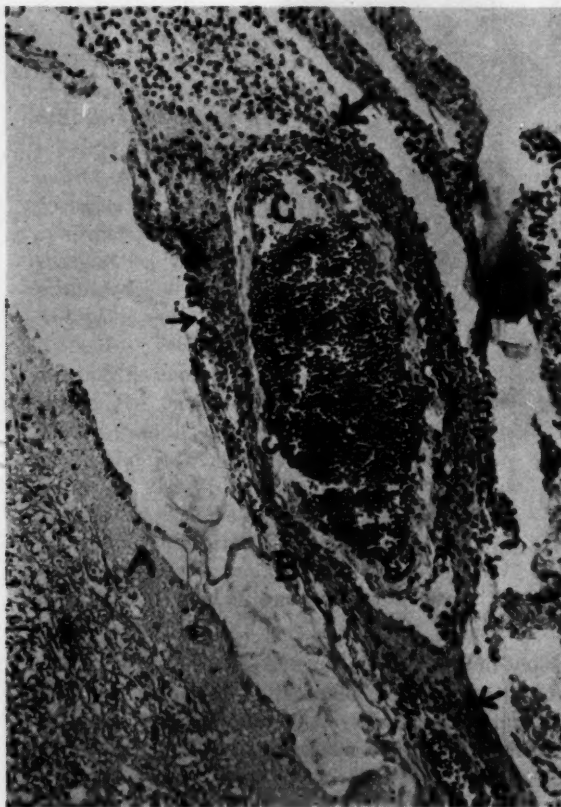

Fig. 2.   Fig. 3.

Fig. 2.—Photomicrograph of the basal portion of the brain (A) showing meninges (B) with thick collars of purulent exudate (arrow) enveloping blood vessels (C). (×100.)
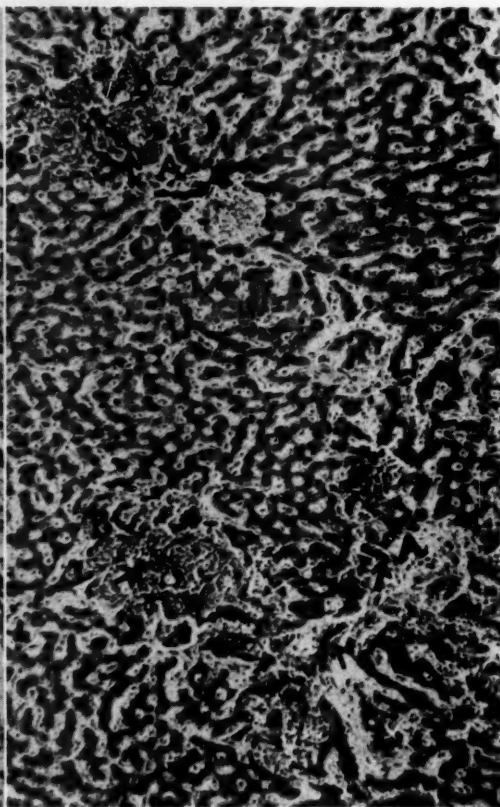
Fig. 3.—Photomicrograph of azocarmine stains of the liver showing large areas of necrosis in the periportal (A) and mid-zonal (B) sections of the lobule. These areas contain masses of fibrin (arrows) within sinuses. (×100.)

Note: Upon recovering the meningococcus from the mother, an attempt was made to culture the viscera and blood of the retained tissues from the body of the baby which had been autopsied on the previous day. Although gram-negative diplococci, morphologically resembling Neisserian organisms, were observed on the direct smears, the cultures were overgrown with *B. coli.*

Anatomic Diagnosis.—1. Meningococcus meningitis. 2. Massive hemorrhage of adrenals, bilateral. 3. Focal fibrinoid necrosis of liver (periportal and mid-zonal). 4. Glomerular ischemia with capillary thrombosis: Interstitial nephritis, focal. 5. Acute splenitis. 6. Hemorrhagic necrosis of epiploon. 7. Pulmonary embolus (osseous); hydrothorax, right; compression atelectasis of right lower lobe; apical scars, bilateral, fibrous. 8. Postpartum uterus with retained secundines; corpus luteum of gestation. 9. Eosinophilic hyperplasia of pituitary.

Comment.—The intriguing problems presented by this case are (1) the asymptomatic meningitis, (2) its differentiation from the coexisting pre-eclamptic toxemia, and (3) the possible relationship between the shock episode and the massive adrenal hemorrhage. The meningitis was unsuspected in this case because the cardinal signs of this disease were absent. Perhaps the most misleading finding was the completely afebrile course of the patient until the last day of her illness. The headaches were attributed to the toxemia of pregnancy, since it antedated by weeks the acute infection discovered at autopsy. The mental changes were believed to be psychogenic and related to parturition. There were no neurologic signs, including convulsions (despite the coexisting lesions of eclampsia), nor were there any petechiae noted. This is quite in contrast with the findings in the series of 16 cases of Waterhouse-Friderichsen syndrome reported by Ferguson and Chapman,[5] in which a petechial rash was observed in 93.7 per cent of the cases and some form of neurologic manifestation in nearly 60 per cent of the patients. Were it not for the finding of massive adrenal hemorrhage, notoriously associated with meningococcemia, the presence of the Neisserian infection would not have been suspected, because neither meninges nor spinal fluid appeared abnormal even at necropsy, until the microscopic examination disclosed the organism.

The sudden, unexpected episode of deep shock which occurred shortly after delivery was probably due to the overwhelming meningococcus infection, with its massive destruction of the adrenals and acute insufficiency of the latter. However, recent observations, such as those by Martland,[6] Moritz and Zamcheck,[7] as well as others, have thrown some doubt on the earlier contention that the adrenal hemorrhage is responsible for the shock associated with Waterhouse-Friderichsen syndrome, similar instances having been encountered in which no adrenal pathology could be demonstrated. They conclude, therefore, that the state of shock and the sudden death in these cases is due more to the overwhelming toxemia than to the acute insufficiency of the adrenals. While it must be granted that in those instances in which adrenal pathology is absent the adrenals cannot be implicated, this does not exonerate them in instances in which massive hemorrhage of the organ does occur. Moritz and Zamcheck found adrenal hemorrhage in as many as 72 per cent of their 81 cases of sudden death from meningococcemia. Had they also included the 14 cases in which they found cortical degeneration, and the 4 cases which showed focal hemorrhages, the incidence of adrenal involvement would be 75 and 94 per cent, respectively. These statistics and the findings reported by previous observers[8] seem to support the earlier contention that the adrenal pathology probably *does* play an important role in the sudden and unexpected deaths in many of these patients. In our case, also, the possible relationship between the massive hemorrhage found in both adrenals and the patient's sudden shock and unexpected death cannot be disregarded.

Summary and Conclusions

1. A rare case is reported of meningococcus meningitis with massive bilateral adrenal hemorrhage (Waterhouse-Friderichsen syndrome) complicating pre-eclamptic toxemia and terminating fatally for both mother and offspring.

2. Several unique features which the case presents are discussed. The meningitis found at autopsy was unsuspected clinically because none of the cardinal signs of the disease were present, except for a rise in temperature during the patient's terminal 24 hours. The classical liver and renal lesions of eclampsia found at autopsy confirmed the clinical diagnosis of toxemia of pregnancy. The meningitis was apparently a terminal complication. There appears to be no similar case ever reported.

3. The literature on meningococcus meningitis complicating pregnancy is reviewed and the relationship between massive adrenal hemorrhage and sudden death in the Waterhouse-Friderichsen syndrome is discussed. While it is conceded that overwhelming sepsis itself may cause shock and sudden death, nevertheless, it is the contention of the authors that in this case, as in cases previously reported by others, the massive adrenal hemorrhage contributed in large part to the profound shock as well as to the sudden and unexpected death of the patient.

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ECLAMPSIA IN THREE GENERATIONS OF THE SAME FAMILY

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RECENTLY the author delivered a young woman who developed postpartum eclampsia. Subsequently, relatives told of other cases of eclampsia in the immediate family. As cases of familial incidence of eclampsia have not been found in the literature, except an instance in a mother and four daughters all of whom died with eclampsia, mentioned by DeLee,[1] it was thought that these cases should be reported.

CASE 1.—Mrs. F. P., a 23-year-old para 0, gravida i, was first seen on Oct. 10, 1951. Her past history was negative except for the usual childhood diseases. Physical examination was normal. Her last menstrual period had been Aug. 24, 1951. The prenatal course was normal with blood pressure varying from 105/70 to 128/80. She gained a total of 18 pounds and at no time had albumin in the urine. Kline and Mazzini tests were negative and she was also found to be Rh negative. On the last prenatal visit, June 2, 1952, the blood pressure was 120/80, weight 150 pounds, no albumin in the urine, no edema, the fetus was in left occipitoanterior position, fetal heart normal and the fetal head engaged.

On June 5, 1952, the patient went into labor following spontaneous rupture of the membranes. As she was quite desirous of keeping sedation to a minimum, the only sedation she received during labor was two 50 mg. doses of Demerol. After 12 hours of labor she delivered, spontaneously, with a mediolateral episiotomy, a 6 pound, 14½ ounce, living female infant. Following the birth of the child she was given 1 c.c. of Pituitrin intramuscularly. Immediately, she had a convulsion which lasted several minutes. She was given ether during the convulsion. The baby showed moderate asphyxia but was resuscitated without great difficulty. A contraction ring of the uterus developed with retention of the placenta. The placenta and membranes were expelled during an attempt to remove the placenta, manually, under an ether anesthetic.

On her return to her room she was alert, her blood pressure was 135/95 and a catheterized urine specimen showed 1 plus albumin. She was given 500 c.c. of 20 per cent glucose in distilled water and sedation with phenobarbital. She had no more convulsions. During the following day the blood pressure varied from 130/84 to 170/100 at which time she had a headache. At that time she showed 1 plus edema in the right foot. Following this, the blood pressure decreased to 130/90 at which time she was discharged from the hospital and showed no albumin in the urine and no edema. On June 28, 1952, she had no complaints, no albumin in the urine, and the blood pressure was 110/70.

CASE 2.—Mrs. V. R., the daughter of Mrs. F. K. and the aunt of Mrs. F. P., had her first pregnancy in 1927 at the age of 30 years. She had albumin in the urine for two or three months before going into labor and also had slight blurring of vision and marked swelling of the feet. She does not recall the blood pressure readings. She had one convulsion immediately after the birth of the baby and several others, possibly 4 or 5, but information on this point is not definite. The baby was stillborn with the cord around his neck. She had two subsequent, normal, uneventful pregnancies and is now in good health. She has at no time had any albumin in the urine since. (This history was obtained by correspondence with Mrs. V. R. and her sister.)

CASE 3.—Mrs. F. K., grandmother of Mrs. F. P., and mother of Mrs. V. R., was pregnant for the first time in 1896 at the age of 23 years. Her health, previous to her pregnancy, was good. During the latter part of pregnancy, she states, she was "bloated from head to foot." She does not remember having any abdominal pain or blurring of vision before going into labor. She had no convulsions before going into labor. The exact time of onset of the convulsions has been rather hard to determine, but it seems that she had several convulsions before the birth of the baby and one convulsion twenty-three hours after the baby was born, followed by several others for a total of nine convulsions. Delivery was apparently normal and the baby (Mrs. V. R.) was born alive and had no neonatal difficulty. Her second pregnancy was apparently uneventful with the delivery of a full-term baby, eleven months after the birth of her first child. The baby died the following day of unknown cause. Her health between her first and second pregnancies was good and her four pregnancies, subsequent to the stilbirth, were normal. There is, of course, no record of the presence of albumin or blood pressure readings during any of her pregnancies. At the present time she is in good health, except for arteriosclerotic changes. (This history was obtained by personal interviews with Mrs. F. K. and a neighbor at the time of her first pregnancy.)

Summary

Three cases of eclampsia occurring in three generations of the same family have been presented. All three patients survived and are living today and two of the babies survived. None of the patients has been left with any residual involvement of the renal or cardiovascular systems. This raises the question of a possible familial predisposition to the development of eclampsia.

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SURGICAL CORRECTION OF COARCTATION OF THE AORTA IN PREGNANCY*

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THIS is a report of a congenital cardiovascular complication in an otherwise normal pregnancy.

The patient, a 20-year-old white gravida ii, para i, entered our prenatal clinic on Aug. 8, 1951, with an intrauterine pregnancy of approximately two and one-half months' gestation. Her past obstetrical history included a 5½ pound stillborn male infant on Oct. 20, 1950, the result of marked hypertension, proteinuria, and complete placental abruption.
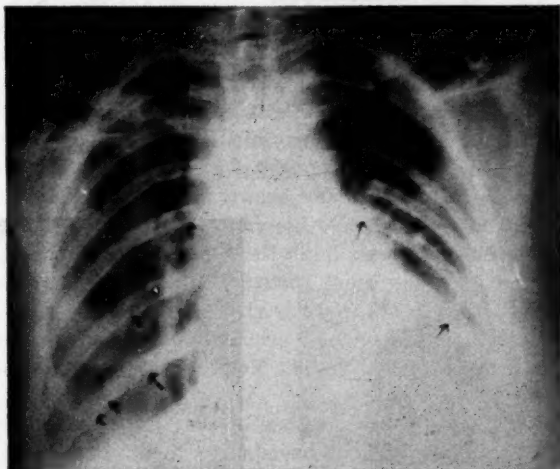

Fig. 1.

On admission to the clinic the significant physical findings were as follows: Blood pressure, arms, 170/100, legs 60/0; Grade II systolic murmur maximal over the pulmonic area but well transmitted down the spine; marked intercostal arterial pulsations of T_4 and above; very feeble and delayed lag of both femoral and popliteal arterial pulsations with absent dorsalis pedis; both lower extremities cold to touch.

The patient was promptly admitted to the Presbyterian Hospital for complete study. The provisional diagnosis was coarctation of the aorta. The blood chemistry was normal. The chest film demonstrated marked notching of the lower rib margins (Fig. 1).

On bed rest her blood pressure recordings fluctuated from 170/110 to 150/100. The urine was negative. Direct arterial pressure studies made by our cardiovascular laboratory confirmed the diagnosis of coarctation of the aorta (Fig. 2). Eye-ground examinations revealed moderate retinal arterial narrowing.

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*Presented before the Chicago Gynecological Society, March 21, 1952.

On Sept. 29, 1951, at four months' gestation, the coarcted segment of the aorta (Fig. 3) was resected at the level of T₄ (Fig. 4). Her recovery was uneventful and the immediate postoperative blood pressure was recorded as 95/55 without signs of shock. This level gradually rose and stabilized at an average of 130/80.
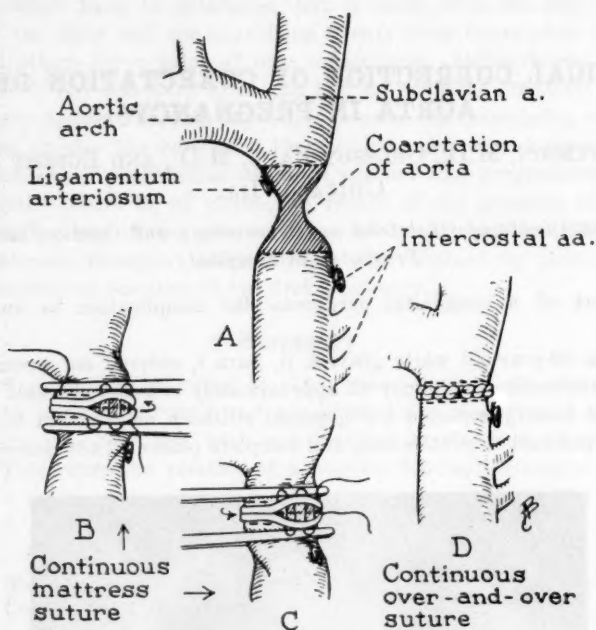

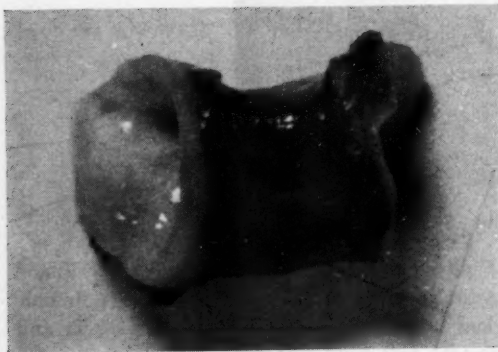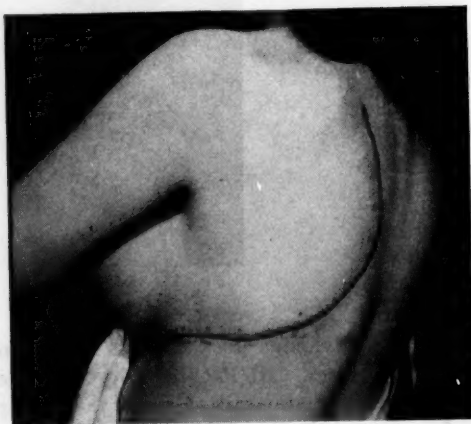Fig. 2.

Fig. 3.   Fig. 4.

Her pregnancy was terminated on Feb. 8, 1952, with a spontaneous delivery of a term 8 pound normal female infant. The highest systolic pressure recorded during the height of labor was 160/100. The patient was discharged on the fifth puerperal day with a recorded blood pressure of 135/90.

55 EAST WASHINGTON STREET
122 SOUTH MICHIGAN AVENUE
5 SOUTH WABASH AVENUE

SARCOMA BOTRYOIDES OF THE CERVIX*

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THE report of this case seems worth while because of the rarity of the disease, its predilection for the younger age group, and the malignant nature out of all proportion to its histological appearance. The standard textbooks of gynecology, pediatrics, pathology, and cancer dismiss the lesion with a few sentences. McFarland's work in 1935[1] is still the standard reference. Since that time little has been added to the histogenesis. Most reports have been case studies with reviews, and I have been unable to find any related to the cervix in the younger age group. Most studies have been made on lesions arising in the vagina and in the main have been pathologic studies.

In a review of 94 mixed mesodermal tumors of the uterus Glass[2] found 58 in the body and all were postmenopausal. The 36 cases in the cervix were in the active sexual period. In this review the cervix was involved 4 times below the age of 10, and 10 times below the age of 20.

Case Report.—This 15-month-old child was admitted Jan. 21, 1951, to the hospital for investigation of a mass protruding from the introitus. There was some confusion about the history as taken from the parents. It was stated that there was something protruding from the introitus when the child was born, but disappeared shortly after. Later it reappeared at approximately 6 months and this was removed by the family pediatrician, who stated that it appeared to be a blood clot and there were apparently no tissue elements involved in the mass. However, the mass reappeared one and one-half months ago, and appeared to be much larger. The appearance was apparently intermittent, depending upon the position of the child. There was bright red blood present in the vagina on one occasion. The child had progressed normally, physically and mentally, and apparently was not inconvenienced by the growth. On local examination there was a moderately large reddish, soft, irregular, grapelike mass protruding directly through the vagina. It oozed blood easily when touched. There was some cyanosis and some apparent degeneration of the surface of the mass. Rectal examination: No remarkable findings were noted other than a suggestion of a mass anteriorly.

On examination under anesthesia (Fig. 1) a large polypoid degenerating mass was found extruding from the vagina which appeared to originate at the internal os. With a nasal speculum, the cervix was visualized and brought down to the introitus. A section taken for biopsy proved to be malignant tissue. The remaining tissue was then excised and the cervix now appeared to be very patulous and filled with tumor tissue. A sound passed a distance of 1½ inches into the uterus. At that time the cervical canal was sutured, controlling all bleeding. On further pathological examination it was found to be sarcoma botryoides, probably originating from the cervix. With this diagnosis, a total hysterectomy was then performed, with removal of approximately one-half of the vagina and most of the broad ligaments. X-ray of the chest was normal on admission.

Diagnosis.—Sarcoma botryoides of the cervix.

Biopsy.—A portion of soft, light tan tissue having a grapelike structure and covered with thickened membrane which in some areas was ulcerated and hemorrhagic.

Microscopic Section (Fig. 2).—This revealed a sarcoma composed of moderate-sized, roughly rounded, or somewhat angular cells with scanty cytoplasm and large vesicular nuclei. The cells were closely packed for the most part but in many areas there was edematous

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or myxomatous tissue. In one section there was an island of cartilage. The periphery of
the tumor was covered by columnar or cuboidal epithelium. There was severe superficial sub-
acute inflammation.

The uterus was normal in size, the vaginal mucosa glistening. The cervix showed
a small nodule.

The cervix showed in one area a cellular somewhat myxomatous stroma with numerous
oval or slender cells similar to the cells found in the grapelike portion of the tumor. The
involved portion was quite superficial and the growth of the tumor was obviously outward.
Invasion of the adjacent stroma was absent. The uterus revealed an intact endometrium.
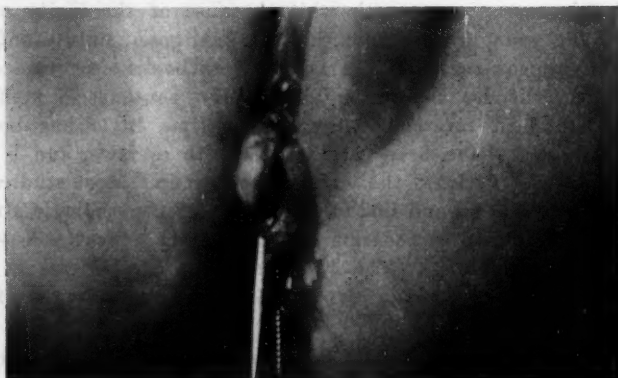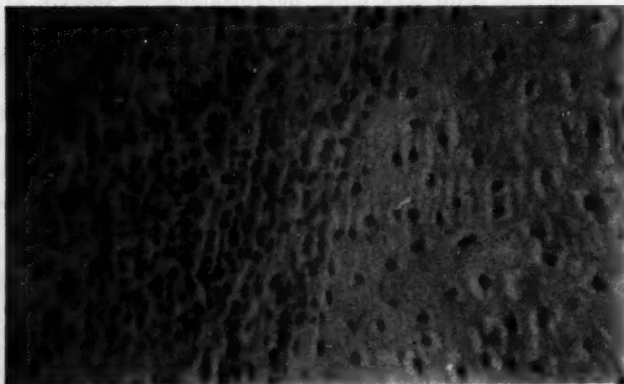

Fig. 1.

Fig. 2.

From all criteria of tumor surgery it would seem that one could promise a good result
in this case. The tumor has been removed. There is no evidence of invasion in the tissue
removed. The experience of the literature is against this optimistic outlook. All of the
patients with vaginal tumors have had local recurrence regardless of the therapy: surgery,
electrodissection, radium, and x-ray. The patient treated by Ulfelder[3] in 1947 with hysterec-
tomy and total colpectomy is still living. All of those with cervical invasion have died.

The follow-up on this case is too short to offer any opinion on the proper management
of such cases.

Examination under anesthesia 18 months postoperatively shows no residual disease.

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420 SLATER BUILDING

SARCOMA BOTRYOIDES

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SARCOMA botryoides is a rare and highly malignant pelvic tumor occurring in the cervix, uterus, and vagina. Although complicated terminology and incorrect identification of individual sarcomatous growths have made the literature confusing, approximately one hundred cases of this tumor have been recorded to date. The following case is presented for its clinical and pathological interest.

Case No. 31625, a 58-year-old white gravida ii, para ii, was admitted April 7, 1951, to Harper Hospital with a history of a blood-tinged watery vaginal discharge of three weeks' duration. During a slight coughing episode, the patient felt something drop in the vagina. This sensation was associated with a profuse vaginal hemorrhage and lower abdominal pain. On examination, the entire vagina was filled with a lemon-sized, polypoid mass which bled very easily. The growth was attached to the cervix with extension to the right vaginal fornix. The grapelike mass was pinkish in color and gelatinous in consistency. On April 9, 1951, under Pentothal anesthesia, the 5 cm. neoplastic growth was severed from its attachments within the vagina and anterior lip of the cervix by a cautery knife (Fig. 1).

Microscopic sections of the removed tissue showed a markedly polypoid neoplastic growth covered by normal squamous epithelium (Fig. 2). Several areas had become ulcerated and secondarily infected. The growth proper was comprised of mesenchyme-like cells with irregular hyperchromatic nuclei and long stellate or linear cytoplasmic processes (Fig. 3). Interstitial spaces contained a structureless gray myxoid material. The core of cells in the central portions of the polypoid projections and at the invading margin tended to assume the appearance of an undifferentiated round-cell sarcoma showing large, bizarre, smudgelike nuclei, scant cytoplasm, and marked lack of uniformity. Only an occasional mitotic figure was present. Vascular spaces were prominent and lined by endothelial cells distinguishable from the tumor cells. Lymphatic spread was obvious with masses of tumor cells present in lymph spaces some distance from the invading tumor margin. There was no evidence of blood-vessel invasion. On the basis of gross and microscopic findings a diagnosis of sarcoma botryoides of the cervix uteri was made.

On April 15, 1951, a panhysterectomy with bilateral salpingo-oophorectomy was performed. An attempt was made during the surgery to remove the upper two-thirds of the vagina since malignant invasion was noted in this region. There was no gross evidence of any malignant extension within the peritoneal cavity. Cross-sectioning of the uterus revealed a 10 cm. tumor mass arising from the lower aspect of the inner wall on the right (Fig. 4). The tumor was soft in consistency and contained evidence of hemorrhage and degeneration. The microscopic picture was comparable with that given in the previous report. Sections through the main mass of tumor tissue revealed normal endocervical glands embedded in the sarcomatous stroma. There was no evidence of malignant transformation of the epithelial glands that had apparently been carried along by the expansile growth of the sarcoma.

One month after discharge, on May 27, 1951, the patient re-entered the hospital complaining of enlargement of the abdomen and recurrence of vaginal bleeding. On examination a recurrent grapelike polypoid mass was seen protruding at the introitus. The mass at this time was found to be attached to the anterior vaginal wall from the urethra to the vaginal cuff with apparent infiltration into the bladder base. There was no

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grossly malignant growth in the right vaginal fornix where it had been noted one month previously. Under Pentothal anesthesia, the major portion of the mass was excised and the vagina packed to control bleeding. Microscopic findings were identical with those of the original biopsy. Deep x-ray therapy was given daily from May 29, 1951, to June 21, 1951, with a total tumor dosage of 2,479 r being delivered through anterior and posterior pelvic ports. Discontinuation of the roentgen therapy was necessitated by the rapid deterioration of the patient's condition. She died at home on July 30, 1951, five months from the time of the original symptoms.

At autopsy the body appeared to be that of an elderly white woman. The skin and subcutaneous tissues showed evidence of emaciation with marked loss of turgor and atrophy of adipose tissue. The abdomen was slightly distended and doughy on palpation. There was a well-healed midline suprapubic surgical scar. Examination of the vagina showed a soft polypoid growth, 4 cm. in diameter, arising from the right lateral wall. There were no jaundice and no significant lymphadenopathy.
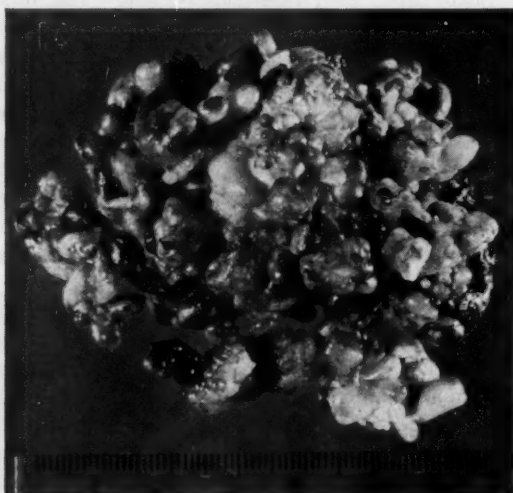

Fig. 1.—Photograph of original neoplastic mass found within the vagina.

Upon removal of the chest plate, inspection of the pleural cavities revealed minor adhesions, but no free fluid. The parietal surface of the chest cavity was studied with numerous subpleural, soft grayish nodules, varying in size from 1 to 4 cm. These soft neoplastic masses were found in the posterior mediastinum and in the periaortic region from the diaphragm to the thoracic inlet. Numerous nodules were also present beneath the visceral pleura of the lungs.

Upon opening the abdomen a very small amount of clear fluid was encountered. Omental adhesions were present at the site of the midline surgical scar. The subperitoneal region of the mesentery was studded with grayish nodules many of which were pedunculated. Inspection of the pelvic area revealed a mass of tumor tissue, very soft and friable in consistency, filling the right lateral portion of the pelvis and invading the periosteum of the sacrum. The periaortic lymph chain showed many large metastatic lesions. At the lower border of the esophagus, approximately 1 cm. from the cardiac orifice, a 3 cm. nodule projected into the lumen causing a nearly complete esophageal obstruction. The right kidney pelvis and ureter were markedly dilated. The right ureter at the level of the ureterovesical junction was completely obstructed by the neoplastic mass. The left kidney appeared grossly normal.

Microscopic findings on the autopsy material showed further anaplasia of cells in the metastatic lesions, the majority of which had lost the myxoid element and were mainly cellular.

A marked variation in cell size, nuclear chromatin content and distribution, and in nuclear-cytoplasmic ratio was noted. Extreme pleomorphism was present in some areas with many giant and multinucleated cells. There was an absence of any organized stromal pattern.

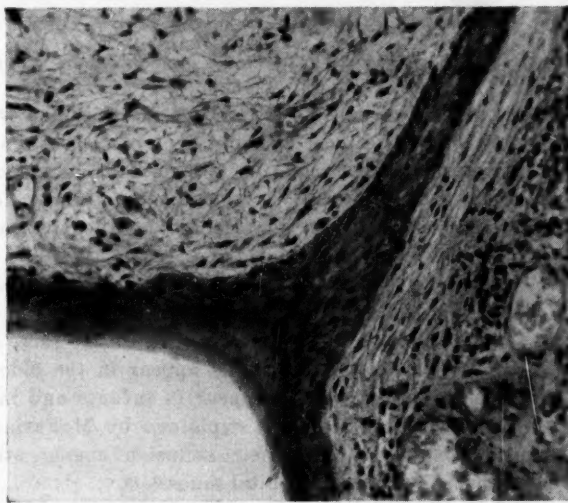Fig. 2.—Photomicrograph of the neoplastic growth. (×10.)

Fig. 3.—Photomicrograph showing the mesenchyme-like cells with irregular hyperchromatic nuclei and long stellate cytoplasmic processes. (×150.)

Areas of cystic degeneration and necrosis were numerous. Pleomorphism and degeneration were more prominent in sections taken from metastatic lesions located in previously irradiated areas. Metastases from within the thorax had a more uniform appearance of undifferentiated large round-cell sarcoma. In no area examined was there sufficient differentiation of cells to warrant a more definitive diagnosis. Metastatic spread of the neoplasm had been entirely lymphatic. The kidneys, adrenals, spleen, liver, and actual lung parenchyma were free of metastases. The final pathological diagnosis was sarcoma botryoides of the cervix uteri with multiple lymphatic metastases.

Comment.—The descriptive term sarcoma botryoides was first applied by Pfannenstiel in 1892; the first case, however, was described by Wagner in 1854. Spiegelberg described the lesion in 1897 as "Sarcoma colli uteri hydropicum papillare."[16]

Sarcoma botryoides has been characterized by the gross appearance of a polypoid grape-like mass arising from the cervix, corpus, or vagina. The tumor appears as fleshlike pinkish edematous polyps which are friable and show superficial areas of necrosis and hemorrhage. The neoplasms may be attached to the cervix, anterior or posterior walls of the fundus, or the vagina by pedicles or broad bases, and are first recognized when they present themselves at the introitus. There is much resemblance to a hydatidiform mole.

Fig. 4.—Photograph of uterus with the mass arising from the inner wall.

On cross section, the tumors reveal cystic cavities intermingled with areas of hemorrhage, necrosis, and suppuration. The most common type of tissue is a loose myxomatous-appearing stroma binding the malignant round or spindle cells in a loose network. Histologically, distinction has been drawn between those tumors containing heterologous elements and those which are pure sarcoma. Those containing heterologous elements may contain cartilage, striated muscle, bone, or epithelial glands.

A majority of the reports in the literature have concerned cases observed in infancy. Simpson believes that there is a definite difference in the average age at which the tumor is first seen and in the number of cases reported from each of the three sites, corpus, cervix, and vagina.[12] He believes the tumors of the corpus appear in the older age groups (from 45 to 65 years) whereas tumors of the vagina appear in infants and in young children.

The histogenesis of these tumors has been explained by McFarland as an accidental dislocation of residual embryonal cells and their inclusion among others retaining their normal positions in the formation of the urogenital sinus.[9, 17]

Clinically, first noted is a serosanguineous, mucoid, or bloody discharge with or without a foul odor. As the tumor progresses in size, it fills the vagina and protrudes through the vulvar orifice. As a result of erosion and infection, hemorrhage and necrosis are common complications. The later stages are usually characterized by vesical irritability and rectal tenesmus. The clinical course shows it to be extremely malignant, quickly recurring and progressing locally. Distant metastases are uncommon. Death usually results from pressure on the ureters by the tumor with a resultant hydronephrosis. The average duration of life is less than one year.

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ARRHENOBLASTOMA OF THE OVARY

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ARRHENOBLASTOMA of the ovary is a term that was first applied by Robert Meyer[1] to that group of tumors of the ovary which originated from dormant vestigial testicular tissue. These tumors can show varying histologic characteristics resembling testicular tissue from the highly differentiated to the highly undifferentiated type. These tumors may also produce either defeminizing, masculinizing, or no symptoms.

In recent years many more cases of arrhenoblastoma have been reported than previously. However, few of these cases have had 17-ketosteroid studies. Those that have been reported have generally shown normal values. This, despite the fact that this condition is accompanied by hirsutism and marked enlargement of the clitoris. It had been suggested[2] that this tumor may secrete androgenic substances that are not excreted as 17-kestosteroids. Meigs[3] recently reported two cases in which the 17-kestosteroids had gone as high as 35 mg. per twenty-four hours.

The following case is being presented as a typical case of arrhenoblastoma of the ovary, but showing a markedly elevated excretion rate of 17-ketosteroids.

N. S., a 22-year-old Puerto Rican nulligravida, was admitted to the Bronx Hospital on Dec. 6, 1950. The patient emigrated to the United States seven months prior to admission, and stated that she was married for four years and, although contraceptives were never used, conceptions did not occur.

The menstrual history had been entirely normal until the present illness with the menarche occurring at 10 years of age.

All complaints started two years prior to the date of admission. In August, 1948, the patient had a normal menstrual period lasting three days. On Sept. 28, 1948, she had one day of vaginal bleeding on the date corresponding to that of the expected menstrual period. Since that date there had been no vaginal bleeding.

For the past two years both the patient and her friends had noticed that her voice had become "rougher," and that a marked increase of hair had appeared over her entire body. There had been no change in the breasts or the patient's weight.

On admission to the hospital examination revealed a well-developed, well-nourished woman who did not appear acutely or chronically ill. A marked facial hypertrichosis was present and a male type escutcheon seen (Fig. 1). The voice was deep. Blood pressure was 110/70. No abdominal striae were seen. The lungs were clear to percussion and auscultation and the heart normal to physical findings. The abdomen was soft and no masses were palpable. Pelvic examination revealed a soft, anterior cervix and a small retrocessed uterus which was freely movable. Anterior, in the midline, and slightly to the right was a cystic mass about 12 by 8 cm. which was nontender and partially movable. The clitoris was noted to be enlarged to twice its normal size.

Laboratory findings revealed a hemoglobin of 14.5 Gm. with 4,800,000 red blood cells and 4,000 white blood cells. The urine showed no albumin, sugar, or cells in a catheterized specimen. The sedimentation rate was 26 mm. per hour and the fasting blood sugar 85 mg. per cent. A twenty-four hour urine specimen was collected on admission and this showed a 17-ketosteroid level of 64 mg. per twenty-four hours (normal 11 to 15). The blood Wassermann was negative.

A diagnosis of arrhenoblastoma of the ovary was made and on Dec. 14, 1950, an exploratory laparotomy was performed. On opening the peritoneal cavity a large left ovarian cyst measuring 13 by 9 cm. was found lying beneath the uterus. The cyst wall appeared bluish, shiny, and intact. The uterus was infantile in size measuring about two inches in total length. A left salpingo-oophorectomy was performed.

Fig. 1.—Patient preoperatively, showing marked male-type hypertrichosis.

Fig. 2.—Ovary cut in two showing solid and cystic areas.

Pathologic Report (Dr. Joseph Felsen): "The specimen is a distended, apparently cystic ovary measuring 13 by 9 cm. The surface of the ovary is smooth and glistening, reddish pink in most of the extent but with several small, scattered purplish areas also visible. On section, the ovary is made up of soft, solid, brownish areas separated by numerous locules containing clear, serous, amber fluid tinged with blood (Fig. 2). The fluid measures 240 c.c.

Microscopic: Section of the ovarian tumor reveals several recognizable elements which are closely intermingled in a highly cellular neoplasm. These are arranged in sheets of cells and smaller cell nests or cords. A second component is a large well-formed type of tubule lined by tall columnar cells with clear or slightly granular cytoplasm. Occasional nuclear gigantism is present and mitoses are very rare" (Fig. 3).

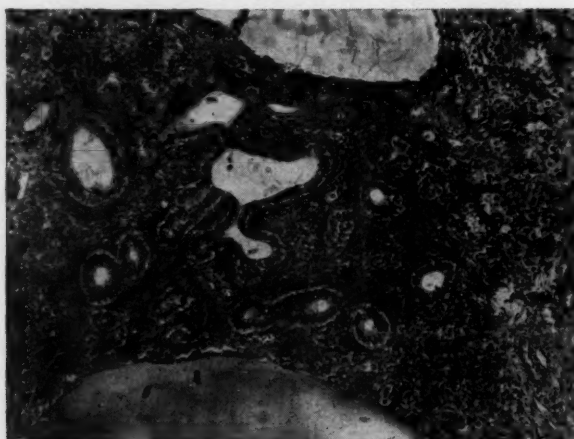The patient had an uneventful postoperative course and was discharged from the hospital on Jan. 6, 1951.

Fig. 3.—Photomicrograph showing solid sheets of cells with interspersed tubules.   (×100.)

On Jan. 28, 1951, the patient was readmitted for a restudy of the urinary excretion of the 17-ketosteroids. The patient stated that on Jan. 15, 1951, thirty-two days following the operation, she had a normal menstrual period, bleeding for four days. The hair over the entire body had been falling out as noticed by hair on the towels when rubbing the skin. There had been no improvement of the voice. The twenty-four hour urine specimen now showed 11.2 mg. of 17-ketosteroids.

Summary.—A classical clinical case of an arrhenoblastoma of the ovary is presented, which is unusual in that the urine showed an exceedingly high level of 17-ketosteroid excretion. This level promptly returned to normal after the involved ovary had been removed.

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          and Stratton.

THECA-CELL TUMOR OF THE OVARY ASSOCIATED WITH A TERM PREGNANCY*

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THIS report has been occasioned by the recent article of Diddle and O'Connor.[1] In a comprehensive review of the literature these authors were impressed with the extreme infrequency of the coexistence of feminizing tumors of the ovary and pregnancy, and also with the hazards involved in such an occurrence. We wish to add this report to a distinctly meager literature.

Mrs. A. McG. was examined initially on March 12, 1951. She was 28 years old and married four and one-half years during which time pregnancy had not occurred. There had been no previous illness or surgery. The menarche had occurred at age 13, the interval varied from 30 to 35 days, and the flow lasted four days with no associated pain. A normal menstrual period had occurred on Feb. 12, 1951.
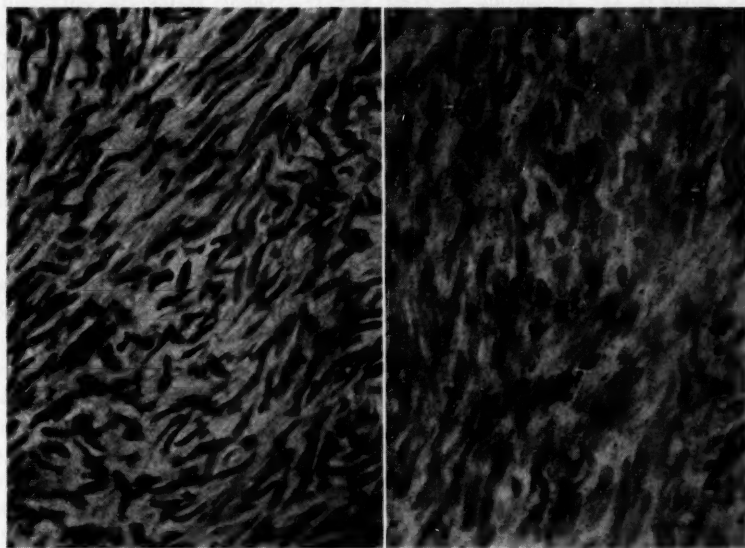

Fig. 1.   Fig. 2.

Fig. 1.—Theca-cell tumor. (Hematoxylin and eosin stain. ×435.)
Fig. 2.—Finely divided intracellular lipid in section stained with sudan III. (×450.)

She was a thin woman of average height, weighed 114 pounds, and was distinctly feminine in type. The basal metabolic rate was plus 10 per cent, and the urine and blood counts were normal. The hymenal opening was less than 1 cm. in diameter and obviously defloration had not occurred. Under local anesthesia sufficient dilatation was obtained to permit vaginal examination. There was no evidence of infection. The vagina was normal in depth and the cervix was normal. The body of the uterus and the adnexa were indistinguish-

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able from a hard, irregular, nodular mass about the size of a ten weeks' gestation and lying in part in the cul-de-sac. The bony pelvis was normal. The diagnosis at this time was multiple uterine myomas and the possibility of pregnancy occurring seemed remote.

Menstruation did not occur in March nor subsequently, and on May 16, 1951, the diagnosis of pregnancy was made. During the following months the tumor remained in the cul-de-sac, obviously obstructing the birth canal, but uncertainty regarding the time of conception delayed an otherwise elective cesarean section.

Labor began following spontaneous rupture of the membranes in the early morning of Nov. 27, 1951. Examination revealed the fetal head displaced very high by the obstructing tumor. A normal male infant weighing 3,380 grams was delivered by low cervical cesarean section under spinal anesthesia. The uterus, the right ovary, and both uterine tubes were grossly normal. A firm white tumor replacing the left ovary and lying in the cul-de-sac was removed. The patient was discharged from the hospital on the tenth postoperative day. Lochia ceased at one month post partum and examination on Jan. 3, 1952, revealed only normal findings.

The gross specimen was 11.5 by 8 by 4 cm. and weighed 193 grams. It was a firm fibrous tissue with a glistening peritoneal surface with an indentation across the midportion. Surfaces made by cutting showed tough fibrillar tissues with mottlings of orange yellow. Microscopic sections (No. 6208 of 1951) were reported by Dr. Edwin F. Hirsch. "The hematoxylin and eosin stained preparations consist of interwoven bands of fibrillar, spindle-shaped cells with considerable collagenous connective tissue. The formalin-fixed tissue stained with sudan has an abundance of finely dispersed intracellular lipid material." The diagnosis was theca-cell tumor.

Sections stained for reticulum showed finely divided reticulum surrounding the individual cells. Under the polarizing microscope doubly refractive crystals were observed. On chemical analysis* of the tumor tissue there were 6.9 mg. of total cholesterol per gram of tissue with 3.4 free cholesterol and 3.5 mg. cholesterol esters.

Summary

A case of theca-cell tumor previa terminated by cesarean section at term is reported.

Reference

1. Diddle, A. W., and O'Connor, K. A.: AM. J. OBST. & GYNEC. **62:** 1071, 1951.

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*Method of Schoenheimer and Spurry.

GRANULAR-CELL MYOBLASTOMA OF LABIUM MAJUS

Fred M. Valentine, M.D., and John R. Thomas, M.D., Houston, Texas

(From the Departments of Gynecology and Pathology, Jefferson Davis Hospital and Baylor University College of Medicine)

MYOBLASTOMA was first described by Abrikossoff[1] in 1926. In 1934 Klemperer[2] reviewed the subject and collected 50 cases with the sites of predilection being the skin, tongue, maxilla, and vocal cords. Powell's[3] paper was the first, apparently, in which involvement of the ovaries was reported.

Howe and Warren[4] reviewed the literature and reported that Geschickter[5] had removed one from the vagina and that Tamis and Kowles[6] and Szathmary[7] had removed one from the labia majora and vulva, respectively. Because of the rare occurrence of genital myoblastoma, the authors wish to add an interesting case.

L. R. (Case X 3538), 54-year-old gravida ii, para ii, Negro, was admitted to Jefferson Davis Hospital on the Gynecological Service on March 19, 1952, with the chief complaint of a growth on the right labium majus. It had been causing slight pain for the previous two weeks. This mass was noted two years before as a small "pimple." It had increased in size slowly over that period of time. No ulceration or drainage from the growth had been noted but there was itching present most of the time. No systemic complaints were registered nor was there any symptom referable to an organ system. The past medical and surgical history was negative. Veneral diseases were denied. Menopause had occurred 14 years before. Obstetrical history was negative.

Physical examination revealed a well-developed, well-nourished adult Negro woman not acutely ill. Blood pressure was 180/120 and cardiac examination revealed left ventricular hypertrophy, a mitral systolic murmur, and an aortic systolic thrill. A stony-hard, nontender, freely movable 2 by 2 cm. mass was palpated in the superior lateral portion of the right labium majus in and immediately beneath the skin, extending into the right paralabial tissue. No ulcerations, fistulas, inguinal adenopathy, or other similar masses were present. Pelvic examination was negative except for senile vaginitis.

The blood Kolmer and Kahn tests were positive 4 plus. Hemoglobin was 13.0 Gm. with a white blood count of 7,000. Hematocrit was 43 per cent and sedimentation rate was 28 mm. in one hour (Wintrobe corrected). The urine was normal.

The preoperative diagnosis was fibroma or chronic inflammatory mass. On March 21, 1952, the mass was excised with the patient under spinal anesthesia. The postoperative course was uneventful and the patient was discharged on March 23, 1952.

Grossly the specimen consisted of three pieces of skin with some underlying subcutaneous tissue. The largest piece measured 2.2 by 1.6. by 1.3 cm. Its surface was rough. The cut surface was pinkish gray and firm. The two smaller pieces were similar. One measured 1.5 cm. in greatest dimension; the other measured 1.0 cm.

Microscopically the dermal and subcutaneous layers were infiltrated by sheets and cords of large polyhedral cells with oval or round nuclei. Most of these nuclei were centrally located and were relatively small compared to the cells (diameters of the cells varying from 20 to 40 microns). The cells had distinct outer membranes delimiting them from their neighbors, except in some instances where the cytoplasm of two or more adjacent cells did not seem to be separated. Such focal groups could be described as syncytial[3] masses of cells. In all of the cells the quality of the cytoplasm was similar. It was pale, eosinophilic, and distinctly granular. Most of the granules were about 1 micron in size and were closely packed together.

No striations were present in the cytoplasm of the cells.

No mitoses were apparent. Nucleoli were present but were not prominent.

No atypism of the cells existed, suggesting benignancy of the tumor.

There is a similarity between these tumors and xanthomas, both grossly and microscopically. However, fat stains in others reported have been negative.[8] Such was the case with ours, none of the cells demonstrating an affinity for sudan III. Thus this particular lesion at least did not appear to be composed of lipophages although the resemblance was striking.

Sweat glands and hair follicles were still present in some parts of the dermal layer but were surrounded by invading tumor tissue. In most places these cells invaded along the spaces between collagen bundles, and replaced the skin appendages. However, there was not complete effacement of normal tissue by the tumor elements even though the latter were widespread throughout the sections. The overlying epidermis was thinned in some areas and thickened (acanthotic) in others. (Some of the previously reported granular-cell tumors have been accompanied by pseudoepitheliomatous hyperplasia of the epidermis.[8] Ours did not have this feature.) Some loss of pigment from the epidermal basal layer of cells into the dermis had occurred. It had been mobilized there by phagocytic cells (melanophages). In no place was there ulceration of the epidermis, although the cells of the tumor extended up to it and impinged against its basal layer in several places. Inasmuch as the lesion was nonencapsulated and granular cells were present at the edges of some of the sections, it appeared that the line of surgical excision cut through edges of the lesion, probably leaving some behind.

Howe and Warren[4] describe the microscopic picture as that of polyhedral cells, 20 to 35 microns in diameter, with fairly well-defined cell membranes and finely granular cytoplasm. The ground substance of the cytoplasm apparently does not take a stain, merely the granules. The nuclei vary in size and are often somewhat vesicular. Nucleoli are present but not necessarily prominent. Mitoses are absent or rare.

There has been much speculation as to the origin of these tumors. Meyer[9] and Roffo[10] suggest that following trauma to striated muscle granular degeneration occurs. They believe regeneration taking place might lead to the development of neoplastic qualities. Gray and Gruenfeld[11] feel that these cells are voluntary muscle fibers undergoing necrobiotic changes.

In support of the idea of a muscle source for these tumors has been the presence of striations in some cells in a few reported cases.[1, 5, 9, 12] This occasional feature helped suggest striated muscle as the possible tissue of origin. At least one case[12] contained granules which appeared to be aligned in the formation of striations.

Tissue cultures of these tumors have been interpreted as growing cells resembling those of striated muscle origin.[13]

The granular element, too, is consonant with the myogenic hypothesis. It is supposed that these particles are in reality embryonic forms of the fibrils found within mature muscle cells.[8] Thus the cells harboring such granules might be considered myoblasts.

The resemblance of the cells to the lipophages of xanthoma is superficial, for whereas the granular-cell myoblastomas are characterized by granular cytoplasm the xanthoma cells are "foam" cells which possess minute vacuoles throughout.[8]

Fust and Custer[14] have expressed the idea that these tumors actually *do not* come from muscle, but instead that they are neurogenic neoplasms. This is based on their occasional occurrence in locations devoid of voluntary muscle; the close association in sections between nerves and these granular cells; and the presence of such cells in some neurofibromas.

Whatever the tissue of origin it is our opinion that this particular labial lesion is neoplastic and locally invasive. However, blood stream or lymphatic metastasis is unlikely, because of its uniform cells, lack of mitoses, nonorganoid and unvarying growth pattern.[15]

Since these neoplasms are radioresistant,[16] the only treatment is that of wide surgical excision. In this case because it appears that all of the lesion has not been excised, a simple hemivulvectomy is contemplated. The patient has not consented to this procedure yet, however.
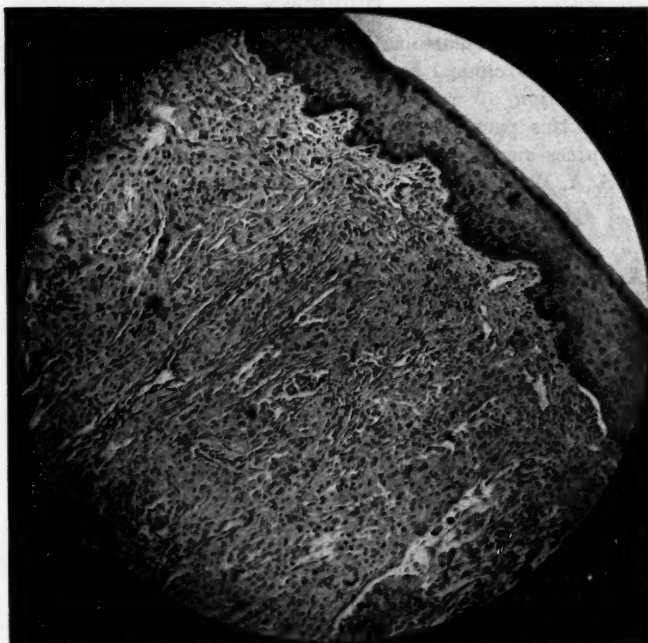
Fig. 1.—Section of skin with diffuse infiltration of the dermal layer by neoplastic cells. (Hematoxylin and eosin, ×120.)
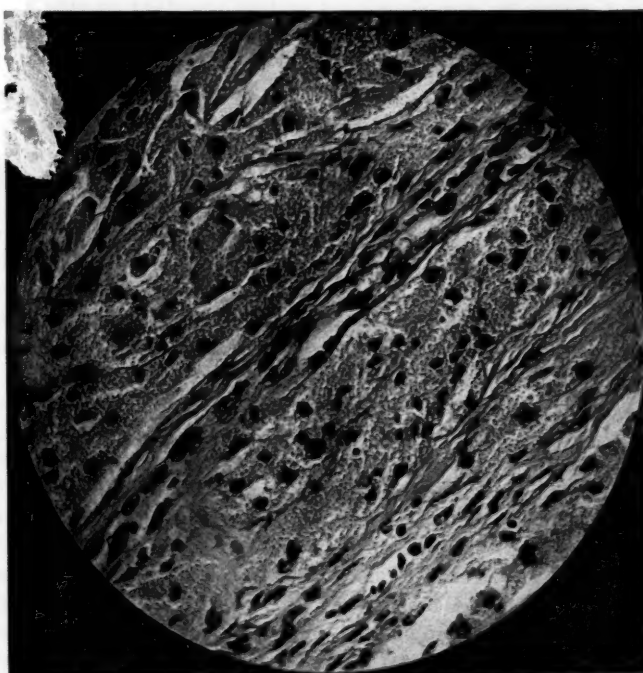

Fig. 2.—High magnification of invading neoplastic granular cells between narrow bundles of dermal collagenous connective tissue. (Hematoxylin and eosin, ×450.)

Summary

A case of granular-cell myoblastoma in an unusual location (the right labium majus) has been presented from both a clinical and pathological standpoint. The mass was surgically excised and up to this time (3 months) there has been no ''recurrence,'' although it is expected eventually in this particular case.

We wish to express our thanks to Mr. F. C. Breckenridge, who made the photomicrographs, and to Dr. S. A. Wallace for his helpful criticism of the text.

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Department of Reviews and Abstracts

CONDUCTED BY GEORGE W. KOSMAK, M.D., NEW YORK

Selected Abstracts

Anesthesia, Analgesia

Gordon, R. A., and Morton, M. Vyvian: Trichlorethylene in Obstetrical Analgesia and Anesthesia, Anesthesiology 12: 680, 1951.

The ideal agent for the relief of labor pains has not been discovered. Such an agent must be successful as an analgesic and/or anesthetic and in addition must be safe for the infant. Drugs that are ideal for the mother may so depress the vital centers, particularly the respiratory, of the infant that their use must be deprecated. Trauma of operative delivery plus analgesia and/or anesthesia adds to the fetal hazard. Premature babies are particularly vulnerable to analgesia and/or anesthesia and, of course, to trauma. Regional anesthesia is less hazardous for the infant but has the disadvantage of "blocking out" the mechanism of "bearing down" in the second stage and, furthermore, there are technical difficulties in its administration which make it impractical for many hospitals and all general practitioners. Realizing the complexities of the problem, the authors carried out a study of an agent they found very satisfactory for obstetrical analgesia and anesthesia; viz., trichlorethylene (Trilene) in the Toronto General Hospital upon 669 obstetric patients. Dr. D. E. Jackson in 1934 was the first to write about trichlorethylene who used it as a general analgesic and anesthetic on dogs in his research laboratory and found it most efficacious. He recommended it for use in human beings. Trichlorethylene is chemically akin to chloroform and resembles it in many of its physical properties. It is noninflammable. Beginning in 1935 it was used sporadically as an analgesic and/or anesthetic in surgery and obstetrics until 1942 when Hewer reported its use in 400 cases to the Royal Society of Medicine. Since that time it has received wide application in Britain and more recently in Canada. Trichlorethylene has proved to be a very satisfactory analgesic and/or anesthetic for use in obstetrics. It has no deleterious effects upon the mother even when used intermittently throughout labor and in combination with nitrous oxide and oxygen for delivery. It is less depressing to the baby than any other inhalation anesthetic hitherto employed in obstetrics. It is satisfactory for all obstetrical procedures except for internal podalic version, where good relaxation of the uterus is required. The usual apparatus employed for other types of inhalation anesthesia is used. The smaller and simpler types of apparatus for use by the patient herself during each labor pain are quite satisfactory. There are a number of different models but all are designed for convenience and safety, thus protecting the patient from overdosing herself. This method of analgesia is quite popular in England, where the question of permitting registered midwives to use trichlorethylene inhalers has been considered by a committee of experts who have laid down certain specifications which, it is believed, will provide an instrument safe enough for such use.

HARVEY B. MATTHEWS

Kaplan, Melvin S., and Arrowood, Julia G.: Prevention of Headache Following Spinal Anesthesia, Anesthesiology 13: 103, 1952.

With the widespread use of spinal anesthesia during the past ten years, a great deal of attention has been paid to the etiology, prevention, and treatment of headache following this form of anesthesia. The authors give a very comprehensive review of this phase of spinal anesthesia. In their own study of the subject their method was twofold. First, a control group of 300 unselected patients who received spinal anesthesia for the usual run of surgical and obstetrical conditions was surveyed and the incidence of headache tabulated. This was noted to be 21 cases, or 7 per cent, of postspinal headache. In 49 obstetric cases there were 6, or 12.2 per cent, and in 251 cases, exclusive of obstetrics, there were 15 cases, or 5.7 per cent. Their technique of procedure is given in detail. The second part of their paper compares the results in another 100 cases of similar surgical and obstetrical procedures using the same technique for the spinal anesthesia but in addition using epidural saline with the idea of preventing postspinal headache. Details of the technique of the addition of epidural saline are given. In this series of 100 comparable cases there was only one case of postspinal headache. The authors claim that the epidural injection of normal saline is innocuous and the technique of administration not difficult. They warn, however, that this is only a preliminary report and further investigation of this procedure, in obstetric patients where the incidence of postspinal anesthesia headaches is highest, should be carried out. There are 4 tables which give excellent statistical details.

HARVEY B. MATTHEWS

Endocrinology

Eichenberger, E., and Hofmann, K.: Hormone Studies in Late Gestation, Gynaecologia 133: 129, 1952.

Considerable work has been done on the quantitative assay of the various hormones of the pregnant woman during the latter part of pregnancy, from the standpoint of both normal and abnormal gestation, as well as from the standpoint of normal and abnormal products of conception. Studies were made on evaluation of estrogens as based on the determination of urinary phenolsteroids, (technique of Bachman and Petit); on chorionic gonadotropins (Aschheim and Zondek) and pregnandiol (method of Huber and Borth). A study of 46 women during the 240-280 days of gestation was made. In general, the antenatal excretion of estrogens, gonadotropins, and pregnandiol can be correlated with the physical condition of the newly delivered child. However, conclusions can be reached to only a limited extent in any single case as to the relationship between viability and normalcy of the intrauterine fetus and the hormone excretion. This was found true because of the wide scattering of all individual values.

L. B. WINKELSTEIN

Torres Morera, A.: Gonadotropinuria in Early Pregnancy, Acta ginec., Madrid 2: 389, 1951.

The author studied the urinary excretion of gonadotropin in 143 pregnant women in the first trimester. The disparity of results obtained was so great that it was not possible to draw more than a hypothetical curve representing the averages of the values found. Gonadotropinuria shows large oscillations, not only in different women, but also in the same woman, values dropping as much as 50,000 or 60,000 frog units within a 48 hour period, only to rise to their previous or a similar level within another day or two. The only uniformity is in the maximal and minimal limits within which the oscillations occur. These limits are under 100,000 frog units as maximum, and over 10,000 as minimum. These figures are for pregnancies between 40 and 100 days of age.

There is, however, a definite tendency to rise at 40 to 45 days of pregnancy, with highest levels between the fifty-second and sixtieth days of gestation.

MAGIN SAGARRA

Bedoya, J. M., and Rodriguez, M.: Do Chorionic Gonadotropins Pass to the Fetus? Acta ginec, Madrid 2: 499, 1951.

The authors studied cord blood specimens of 50 unselected fetuses born at term. The blood was obtained from the placental end upon cutting the cord. Blood samples were also obtained from 9 of the mothers. All tests were performed with the male frog (*Rana esculenta*) by the usual technique. Two and five-tenths to 3.0 c.c. of cord serum were used in each case, and 0.5 to 1.0 c.c. of maternal serum.

Not one of the frogs injected with cord serum ejaculated spermatozoids. All frogs injected with maternal serum did.

The authors conclude that fetal blood, obtained from the umbilical cord, does not contain gonadotropins, or, in any event, would contain them only in minimal amounts. Chorionic gonadotropins, therefore, do not pass to the fetal circulation. This is as it should be, for the following reasons:

1. The trophoblast, where gonadotropins are elaborated, is on the outside of the villi but in contact with maternal blood. The trophoblast is an *exocrine* gland with respect to the fetus, and an *endocrine* gland with respect to the mother.

2. Chemically, gonadotropins are protein compounds of high molecular weight, up to 80,000 to 100,000. We know maternal proteins do not pass directly through the placenta. Therefore, from the chemical composition of gonadotropins, and the known impermeability of the placenta with respect to proteins, it is to be expected that gonadotropins cannot pass the placental barrier.

3. From another point of view, the role of gonadotropins is to compel the maternal organism to provide nutrition to the nidated embryo. On the other hand, the fetus has no apparent need for gonadotropins. So that, teleologically, passage of gonadotropins to the fetus would be useless.

MAGIN SAGARRA

Gynecology

Ahumada, J. C., and Arrighi, L. A.: Metastatic Vaginal Hypernephroma, Obst. y ginec. latino-am. 8: 393, 1950.

The authors, from Buenos Aires, discuss and report on a rare case of renal carcinoma which metastasized to the vagina. It is reported as the second case in Argentinian literature and the twenty-fourth from world literature.

A small nodule was discovered on the right side of the anterior vaginal wall of a 42-year-old woman. This lesion later ulcerated. It was excised and the pathologic report was vaginal hypernephroma. Urological examination revealed hypernephroma at the upper pole of the right kidney. Nephrectomy was performed. The patient was alive and in good health two months after surgery. The world literature is well documented in two tables and four photographs accompany the article.

CLAIR E. FOLSOM

Borras, Pablo E.: Histophysiology of the Ovary, Functional Importance of the Theca Interna, Acta. ginec., Madrid 2: 463, 1951.

The author reviews and supports the investigations initiated by R. Araya concerning the integral function of all ovarian tissue. Araya reached the conclusion that the supposed predominance of the Graafian follicle was an error of interpretation. Investigating healthy adult women, he had been able to observe a large number of cases in which extirpation of the developing or mature follicle, or the corpus luteum, was carried out in the course of a laparotomy for some extragenital affection, without producing any important change in the endometrial cycle. This observation led Araya to believe that it was not the Graafian follicle or its corresponding corpus luteum which was responsible for the cyclic evolution of the endometrium, but rather the rest of the ovary. He was subsequently able to confirm anatomically, histologically, and clinically that the somatic and generative functions of the ovary are two

separate entities: on the one hand, the ovary elaborates a follicle in order to obtain a fertilizable ovum, and, on the other hand, it elaborates an endometrium for the purpose of nidating the fertilized ovum. There is no cause and effect relationship between the follicle which matures and ruptures, and the endometrium which progresses to its secretory progestational phase; these two processes are the result of the same stimulus but are independent of one another.

The author's personal observations confirm the above investigations of Araya. The author notes that cyclic changes are more regular in the evolution of the endometrium than in the evolution of the follicle, and that destruction of the endometrium has a greater effect upon the integral function of the ovary than destruction of a mature follicle.

These facts having been established, it remained to be determined which parts of the ovary were responsible for the development of the follicle and the cyclic changes in the endometrium.

Histologic study of the ovaries of healthy women in their reproductive years immediately reveals a great number of follicles in permanent evolution, in both the first and second phases of the cycle. When these follicles regress and become "atretic," it is precisely then that they acquire their greatest endocrine functional activity, evidenced by the great development of their theca interna. Dubreuil no longer calls these follicles "atretic" but rather "thecogenous," and the sum total of all these follicles in evolution he calls "follicular thecogenous mass." Dubreuil further states that gametogenous follicles (ovum-bearing) are not necessary for an apparently normal menstrual cycle, but it is difficult to conceive of an active ovary without thecogenous (atretic) follicles.

Araya has also pointed out that the great disproportion between the number of follicles which undergo involution and those that produce an ovum indicates that the involuting follicles have, as one of their most important functions, the one of assuring the development of the ovum-bearing follicle.

The author illustrates his thesis with several photomicrographs showing the development and preponderance of theca cells in the ovary. He attaches importance to the presence of lipids in these cells, which he believes are an index of their functional activity.

He concludes that the theca cells constitute the most important functional tissue of the ovary, and that they have the principal role in the estrogenic phase of the cycle. Their functional activity is continuous, the histologic picture being constant throughout the reproductive life of the woman. He recognizes the theca cells as the principal source of estrogens, whether in the developing or mature follicle or in the atretic elements.

<div align="right">MAGIN SAGARRA</div>

Quer, Erich A., Dockerty, Malcolm B., and Mayo, Charles W.: Ruptured Dermoid Cyst of the Ovary Simulating Abdominal Carcinomatosis, Proc. Staff Meet. Mayo Clin. 26: 489, 1951.

As is stated by the authors, dermoid cysts comprise 10 per cent of all ovarian cysts and 10 per cent of these are bilateral. Rupture of a dermoid cyst is rather rare due to the structure and thickness of its capsule but when rupture does occur serious consequences usually result. Preoperative diagnosis is difficult. Upon opening the peritoneal cavity the existing pathology is confusing. Adhesions are extensive and dense. The granulomatous peritonitis is extensive. There is always free fluid present in the peritoneal cavity. This picture simulates both tuberculous peritonitis and abdominal carcinomatosis from which a differential diagnosis must be made. The presently reported case of ruptured dermoid cyst simulating abdominal carcinomatosis, together with a short résumé of the literature, is the fourth such case occurring in the Mayo Clinic. This fact alone would attest to its rarity. In summary, the authors draw attention to the following highlights: (1) Rupture may be sudden or prolonged. (2) The cause of rupture may be obscure. (3) The intraperitoneal pathology following rupture must be differentiated from tuberculous peritonitis and abdominal carcinomatosis. (4) Diagnosis can occasionally be made preoperatively by x-ray since

dermoids often contain radiopaque elements, and by paracentesis. (5) The diagnosis may be suspected at operation by the presence of free fluid containing cheesy or oily material or the presence of oil or hair in the granulomatous nodules. (6) The nodules are not true cysts but pseudocysts in a foreign body granuloma. (7) The treatment of choice is removal of the primary tumor without any attempt to separate the dense and extensive adhesions.

<div align="right">HARVEY B. MATTHEWS</div>

Labor, Management, Complications

Lóránd, S., Szirmai, E., and Csizmadia, Z.:   The Effect of Vitamin B_1 on Activity of Labor and Amount of Pain by Tocographic Analysis, Gynaecologia 133: 155, 1952.

Soviet investigators have felt that the use of Vitamin B_1 during labor increases the force of uterine contractions and decreases the discomfort of labor when given in doses of 40 to 150 mg. intravenously. They state that pain is decreased quickly and that the result is very transient, but when it is given both intravenously and intramuscularly the effect is maintained throughout labor in almost 50 per cent of cases. The authors have tried the use of 50 mg. of thiamine intramuscularly in 50 cases of primiparous and multiparous labor. They feel from their observations of tocographic tracings that the relaxation phase of uterine contractions is not affected, but that active contractions are increased in about 50 per cent of the cases and that labor is definitely accelerated in 38 per cent of the cases. Furthermore, in their opinion, the passive resistance of the lower uterine segment and of the cervix is reduced by the injection of the vitamin. Since the portion of the uterus is felt to be the seat of most pain during labor, the relaxation of these parts decreases the discomfort of child-birth. As Vitamin B_1 did not cause any noticeable detrimental effects on either the mother or the child, the administration of this substance for its analgesic effect and possible acceleration of labor is considered useful.

<div align="right">L. B. WINKELSTEIN</div>

Williams, E. A., and Stallworthy, J. A.:   A Simple Method of Internal Tocography, Lancet 1: 330, 1952.

Various methods of internal and external tocography, and their inaccuracies and hazards are reviewed. The authors describe a new, simple, and convenient method of internal tocography which they term ''The Oxford Method.'' A high puncture of the amniotic sac is made with a curved (Drew Smythe) catheter introduced through the cervix. Through this is threaded a No. 4 Polythene tube with multiple perforations at its end. The catheter is then removed, and the tube remains in position throughout labor, being retained without discomfort or interference with the patient's movements. It measures intrauterine pressures directly, without the need for mechanical adjustments or correction factors.

Preliminary observations reveal a basal intrauterine pressure of 8 mm. Hg. During first stage contractions this rises to 40 to 90 mm. During strong expulsive efforts of the second stage the pressure reaches 120 to 140 mm., and on one occasion was found to reach 180 mm.

<div align="right">IRVING L. FRANK</div>

Cappe, Bernard E., and Pallin, Irving M.:   Treatment of Massive Hemorrhage in Obstetric Cases by Transfusion and Norepinephrine, Anesthesiology 12: 728, 1951.

The development and action of norepinephrine in shock are briefly reviewed. Following this is a brief comment to the effect that hemorrhage remains one of the leading causes of maternal mortality and that if the hemorrhage remains unchecked there is progression to impending shock, shock, and irreversible shock. Of all the measures which have been recommended, the rapid replacement of blood loss remains the basic therapy in the treatment of shock, particularly that following massive hemorrhage. In certain cases of obstetric hemorrhage, even though large quantities of blood are given, shock progresses and finally becomes

irreversible. In cases of profound shock, the authors recommend the use of norepinephrine in conjunction with copious blood transfusions. Three such cases are reported in which 4 c.c. of 1:5,000 norepinephrine were mixed witth 500 or 1,000 c.c. of blood and transfusion given rapidly by positive pressure. In each instance the blood pressure was raised when norepinephrine was added to the blood transfusion. Two of these patients survived and one died, largely because a diagnosis of ruptured uterus and decision to operate were delayed nine hours during which time true irreversible shock developed. The rapid and marked improvement immediately following the transfusion to which norepinephrine had been added would tend to lead to the assumption that the drug was helpful. There were no control studies carried out, thus definite information is lacking as to whether or not norepinephrine was the only agent acting to raise the blood pressure. The results of this study are encouraging and warrant further study by other investigators.

HARVEY B. MATTHEWS

Newborn

Coodin, J. Fischel: Prematurity: A Statistical Study. II, Bull. Margaret Hague Maternity Hosp. 4: 92, 1951.

It is a well-known fact that prematurity is the greatest single factor involved in neonatal mortality. It is responsible for well over one-half of all neonatal deaths which occur during the first month of life.

The problem of prematurity is so important and widespread that a great many studies from all over the world, and particularly from the United States, have appeared in both the obstetric and pediatric literature during recent years. Furthermore, due to the lack of uniformity in hospital statistics on premature infants, many discrepancies have appeared. The author, quoting from a recent article by Helen Wallace and associates, agrees that the chief reasons for these discrepancies are: (1) that the definition of premature infant is not uniform throughout all hospitals; (2) that every premature infant born alive in the hospital is not followed through the hospital until discharge or death; (3) that not all premature infants born alive in the hospital are included in the hospital data. With strict adherence to these criteria, the author reports a statistical analysis of 608 premature infants weighing 2,500 Gm. or less, occurring in 8,414 deliveries at the Margaret Hague Maternity Hospital during 1950. In certain instances comparisons are made of these results with similar studies ''across the country.'' There are six statistical tables which give in detail the outcome of these 608 premature infants. Five deal successively with neonatal mortality rates in relation to birth weight and sex; birth rate and race; birth rate and period of gestation; and the type of delivery. Table VI gives the time of death in infants who died. Of the 90 prematures who died (14.8 per cent) only 22 came to autopsy, a rate of 24.4 per cent. This is an extremely poor autopsy showing, says the author, and something should be done about it. Eighty per cent of the deaths in this series occurred within 48 hours of birth—the ''critical period'' for the premature infant. Strangely enough, in this series, maternal complications did not seem to influence fetal mortality adversely, particularly as regards toxemia of pregnancy, a condition usually regarded as very deleterious to the premature infant.

HARVEY B. MATTHEWS

O'Brien, D.: Terramycin in the Prophylaxis of Ophthalmia Neonatorum, Lancet 1: 347, 1952.

Ophthalmia neonatorum is defined in this study as ''a definite purulent conjunctivitis.'' Gonorrheal ophthalmia is encountered very rarely at the author's hospital, and the value of terramycin in its prevention was not separately evaluated. Five hundred twenty-four newborn infants were treated prophylactically with eyedrops containing 5 mg. of terramycin per 100 ml., or with ophthalmic terramycin ointment containing 1 mg. per 100 Gm. A control series of 523 infants was treated by simple wiping of the eyelids with sterile lint. The in-

cidence of ophthalmia was substantially the same in the treated and in the control series. The author concludes that terramycin is of no value in the prevention of ophthalmia neonatorum.

<div align="right">IRVING L. FRANK</div>

Pregnancy, Complications

Hodgkinson, C. P.: Hemorrhage From Ruptured Utero-Ovarian Veins During Pregnancy, J. A. M. A. 148: 277, 1952.

Spontaneous rupture of the uterovarian veins was a rare complication of pregnancy. Sudden unilateral abdominal pain and shock were the important symptoms. The anatomic distribution of the hemorrhage was of three types: retroperitoneal, intraperitoneal, and a combination of both. The over-all maternal mortality was 49.3 per cent. Bleeding confined to the posterior retroperitoneal spaces produces unilateral flank pain. Bleeding into the peritoneal cavity results in evidence of peritoneal irritation that quickly spreads over the entire abdomen. When a combination of intraperitoneal and retroperitoneal bleeding occurs, the symptoms and physical findings are mixed. The pain of labor may obscure the symptoms, and shock from hemorrhage may be the first evident physical finding. Delay in establishing the diagnosis may increase the maternal mortality.

<div align="right">WILLIAM BERMAN</div>

Jennings, Emmit M.: Multiple Primary Malignant Tumors of Rectum and Breast Complicating Pregnancy, J. A. M. A. 148: 736, 1952.

The author reports a case of carcinoma of the breast and rectum complicating pregnancy and reviews the literature on this subject, as well as the literature on multiple tumors. In carcinoma of the rectum complicating pregnancy the author recommends in the first and second trimesters a resection of the lesion by either abdominoperineal resection or section with an end-to-end anastomosis. In the seventh and eighth months he recommends a cesarean section and, depending on the status of the patient, a resection of the malignancy at this time or after two to four weeks; and in the ninth month induction of labor, with delivery from below followed in 2 o 4 weeks by resection, or the procedure recommended for the seventh and eighth months. The uterus is to be removed only if involved by direct extension from the tumor. Delivery from below is to be allowed only if rectal and pelvic findings permit.

Carcinoma of the breast is to be treated by radical mastectomy and deep x-ray therapy regardless of the stage of the pregnancy. If the patient is only a few weeks from term it might be wise to wait until delivery is completed. The author feels that the malignancy should be eradicated and the pregnancy be allowed to continue.

<div align="right">WILLIAM BERMAN</div>

Pregnancy, Physiology, Diagnosis

Bedoya, J. M., Jimenez, V., and Puras, A.: Biologic Diagnosis of Pregnancy by Injection of Blood Serum to Male Frog, Acta ginec., Madrid 2: 495, 1951.

The test proposed by the authors is based on the well-known presence of gonadotropins in the serum of pregnant women. They feel that the use of serum in preference to urine has certain advantages, such as: (a) A renal lesion might prevent passage of gonadotropins in the urine. (b) The serum is less toxic than urine to the frog. (c) Discomfort to the patient is not much greater than if urine is obtained by catheterization. (d) In some cases it may be desirable to perform the test without letting the patient know that a pregnancy is suspected. (e) Blood obtained for serology and other studies can be simultaneously employed for the test.

The authors performed this test on 50 healthy women, of whom 45 were pregnant and 5 not pregnant. The test was positive in all frogs (90) injected with 0.5 c.c. of serum of the 45 pregnant women. The test was, of course, also positive when larger amounts of serum were employed (up to 3 c.c.). The reaction was always negative when serum of nonpregnant women was used. Animal mortality was nil.

The technique is simple: 10 c.c. of blood are obtained and allowed to clot. After retraction of the coagulum enough serum can be obtained for the test. No special preparation or detoxication of the serum is carried out. The frogs are injected and results read in the same manner as when urine is used.

The authors conclude, from their limited experience, that with a dose of 0.5 c.c. of serum results are correct in all cases, and the animals tolerate well amounts up to 3 c.c.

MAGIN SAGARRA

Parks, John: Pregnancy After Forty, Geriatrics 6: 399, 1952.

Pregnancy in older women is more likely to be associated with thyroid disease, obesity, and with hypertensive vascular and renal changes. Chiefly because of these medical complications, in addition to gynecologic disorders of the fifth decade, maternal death is six times as likely to occur from 40 to 44 years of age, and nine times as likely after 45 as it is at the optimal age of 20 to 24. Even so the national over-all mortality rate in women over the age of 40 is less than five per thousand. This increased risk is a function of the medical and local complications; age alone, in the otherwise healthy woman, should have very little influence on the course of pregnancy and delivery. Certain tendencies are, however, statistically apparent: (a) increased incidence of toxemia, (b) an increased incidence of breech presentation, (c) premature labors, (d) poor responsiveness to induction of labor with pituitary extracts, (e) a higher rate of fetal abnormalities, including mongolism, and (f) an impaired tolerance of the postpartum involution period.

On the basis of age alone, cesarean section is rarely indicated, but is preferable to a difficult vaginal delivery.

The author discusses in detail the altered emotional reactions of the older woman, and counsels scrupulous attention to obstetrical and psychological factors.

IRVING L. FRANK

Shaw, Wilfred: The Origin of the Lower Uterine Segment, J. Obst. & Gynaec. Brit. Emp. 58: 165, 1951.

In his studies of the development of the lower uterine segment, the author included a study of the reflection of the peritoneum from the front of the uterus toward the bladder. In his specimens he found that in the normal nonpregnant uterus the site of the reflection is practically at the level of the internal os; fibroids may cause a distortion; early in pregnancy this reflection is displaced upward. By the study of a series of photographs of microscopic sections of the nonpregnant uterus and the uterus in early pregnancy, it was possible to detect the lower limit of the upper segment. This lower edge is cone shaped, and in most cases the apex of the cone is located about two-thirds of the way down the isthmus, although this position varies. No gross change of the myometrium around the internal os was found in the pregnant uterus until about the twentieth week of pregnancy; but the fossa on the front of the uterus is pulled up and there is a growth of decidual tissue downward into the isthmus. Near term, it was found that the muscle wall just above the cervix is thinned, stretched by the fetal head; at the same time there is an upward pull of the condensed muscle layer, drawing the apex of the cone upward. While it could not be determined from study of specimens at what time this change occurs, clinical studies and vaginal examination indicate that, at about the time of "lightening," the head sinking down low into the uterus gives the patient a feeling of relief, as the cone is drawn upward and the tissues below it become distended. When labor begins, the muscle of the myometrium contracts and is drawn upward and as labor advances, especially in cases of obstruction, the apex of the cone is more clearly defined.

When the membranes and the fetus reach the cervix proper, the lower part of the isthmus and the cervix become dilated and stretched to a far greater degree than above the apex of the cone, as their muscle tissue is relativly thin. Thus this study indicates that the apex of the cone should be regarded as the level of the physiological retraction ring.

<div align="right">HARVEY B. MATTHEWS</div>

Ventura, S., and Klopper, A.: Iron Metabolism in Pregnancy, J. Obst. & Gynaec. Brit. Emp. 58: 173, 1951.

Estimations of hemoglobin, serum iron, iron-binding capacity of the serum, serum copper, and free erythrocyte protoporphyrin were made in a group of normal women, in pregnant women in four stages of pregnancy, and in puerperal women from the first to the fortieth day. The findings were compared with those reported by others. In late pregnancy, a definite and significant decrease in serum iron was found, while the iron-binding capacity of the serum, the serum copper, and free protoporphyrin are increased. There was little significant change in the hemoglobin. While these changes do not represent a definite state of iron deficiency, they do indicate a change toward iron deficiency in normal pregnancy. Whether a state of actual iron deficiency will be reached depends upon the iron reserves of the pregnant woman and her ability to absorb iron. If her reserves are poor, she will reach a stage of manifest iron deficiency before the end of pregnancy. The chief cause of the disturbance of iron deficiency in the pregnant woman is the demand of the fetus for iron in the later months of pregnancy.

<div align="right">HARVEY B. MATTHEWS</div>

Toxemia

Schulze, Ernst E.: Prevention and Treatment of Eclampsia With Cholinesterase, Zentralbl. f. Gynäk. 74: 296, 1952.

Doryl (Merck) has been used by the author for approximately twenty years in the treatment of eclampsia and pre-eclampsia, and although records were lost during the war it was felt that over 28,000 cases were treated successfully, of which over 400 were of the most severe variety. Doryl (Merck) is the trade name for carbaminoylcholine chloride. Its action in the body is typical of that of the group of parasympathetic nervous system stimulators and is very similar to the action of acetylcholine. The effect, however, is much stronger than that of acetylcholine, since it is not only more stable, but also is much more slowly excreted. On injection, a lowering of both the systolic and diastolic pressures results from a dilatation of the large arterioles. This is accompanied by a slowing of the pulse rate without change in the minute output of the heart, a marked miosis, an increase in smooth muscle tonus and activity, as well as marked secretion of the digestive and sweat glands. It also produces a profound diuresis. The effect of this drug is nullified by atropine.

When the diagnosis of pre-eclampsia is made, or when sudden changes in the physical condition of the pregnant patient indicate the presence of impending convulsions, the following procedure was immediately undertaken: Doryl, 0.5 mg., was given subcutaneously (never intravenously) and the condition of the patient closely checked for a minimum period of two hours. Blood pressure was recorded every 15 minutes. In most cases a drop in both systolic and diastolic pressures of from 20 to 40 mm. Hg was recorded in from 5 to 25 minutes, together with a definite slowing of the pulse rate. This, however, was found to be transient, in that a return to the previous high level occurred in from 40 to 50 minutes. It was therefore found necessary to repeat the injections after half-hour and one-hour intervals. The reaction to the drug was very marked. In most instances, even after the first injection, the patients complained of profuse perspiration, "goose pimples," severe vomiting, chills, fever, and tremendous salivation, together with intense peristalsis accompanied by the passage of much gas and the passage of profuse watery stools. In every instance a profuse diuresis (3 to 4 L. in 2 to 3 hours) also occurred. All patients complained of severe discomfort. However, all of the subjective complaints of toxemia noted before therapy was started (headache,

spots before the eyes, poor vision, etc.) completely disappeared. If the above reaction was provoked by the initial injection, the amount used in subsequent injections was not increased. However, if the first injection did not induce a satisfactory response, a second dose of 0.75 or even 1.0 mg. was administered. Similarly, if the blood pressure did not remain down after the two-hour interval, injection therapy was continued for twenty-four or more hours. It was noted, however, that, if the blood pressure did not follow the customary pattern, the drug had less effect after twenty-four hours of use than it did initially, a phenomenon which the author thought was due to increased production of cholinesterase or "noradrenalin." However, he states that in these cases the blood pressure elevation was not significant and the danger of eclamptic seizures was over.

Similar therapy was followed in all cases of toxemia of pregnancy whether pre-, intra-, or post partum. If labor occurred or was in progress and the patient was deliverable from below, this was the procedure of choice, with all precautions taken to aid and facilitate the delivery and minimize the amount of trauma. However, if it appeared that labor would be delayed, prolonged, or traumatic, the author advised cesarean section, primarily in the interests of the child. If, however, the conceptus was dead in utero, the small doses of Doryl mentioned above were ineffectual and much larger doses were necessary to prevent eclamptic seizures. Similarly, in postpartum eclampsia, larger doses (0.5 mg.—1.0 mg.—1.25 mg.) were necessary to prevent untoward symptoms. Supportive therapy, including saline and glucose infusions, sedation, and gastric lavage, is also indicated.

Although results cannot be completely evaluated because of the loss of complete records, very few maternal deaths are remembered. No cases of fatal poisoning or drug toxicity deaths were found when Doryl was used. Doryl had no effect on the fetus other than a temporary slowing of the fetal heart rate, and no intrapartum or neonatal deaths could be attributed to its use. In conclusion, the author states that the use of Doryl is not harmful to either mother or child. He bases the rationale of the treatment upon the decrease in the blood pressure, together with the marked loss of fluid through all possible channels of the body. As the result of these, edema of the brain is relieved, and convulsive seizures thus prevented. He further states that the loss of fluid is probably accompanied by the removal of toxins from the body, which toxins are the ultimate cause of the toxemic state. Liver and kidney damage are thus minimized. The author states that in his opinion Doryl is the most efficacious choice in the treatment of toxemia of pregnancy, and is able to replace all other methods of treatment.

                                                                      L. B. WINKELSTEIN

McCall, Milton L., and Taylor, Harry W.: Effects of Barbiturate Sedation on the Brain in Toxemia of Pregnancy, J. A. M. A. 149: 51, 1952.

This study shows that amobarbital sodium and thiopental sodium, intravenously administered in minimal doses to cause unconsciousness, bring about marked change in cerebral function in toxemic pregnant women. On the other hand, phenobarbital sodium administered intramuscularly in large doses caused neither clinical effect nor significant change in cerebral function. The cerebral oxygen metabolism was the function most affected. Theories as to the causes for this depression of cerebral oxygen are mentioned. The depressions brought about by coma and anesthesia are pathological. In addition to the histotoxic anoxia present during the comatose stage of eclampsia, there is also anoxic anoxia due to the respiratory difficulties during the convulsion. It is therefore evident that eclampsia is a disease associated with oxygen deprivation and deficient uptake of oxygen by the brain during the convulsive stage and a compromised cellular oxygen metabolism in the presence of normal oxygen supply during the comatose phase.

                                                                      WILLIAM BERMAN

Correspondence

Effects of Cortisone on the Fetus

To the Editor:

We thought the results of cortisone on the fetus when administered during the first trimester of pregnancy would interest the readers of the JOURNAL. The drug was administered to thirty patients during the first trimester of pregnancy for nausea and vomiting. We were therefore given the opportunity to observe these patients during the remainder of the pregnancy and delivery. The average dosage of cortisone used was 50 mg. per day by mouth, and, of the thirty patients treated, twenty-eight delivered here. The other two delivered normal babies elsewhere.

Complications were as follows:

1. One baby had a club foot.

2. One baby had a persistent heart beat of 60 to 80 per minute during pregnancy. The infant lived three days and had heart block by electrocardiogram. Autopsy revealed coarctation of the aorta.

3. One baby was delivered at 32 weeks' gestation, weighing 4 pounds, 15 ounces, and died on the third day of life for no apparent reason. Autopsy was negative except for atelectasis.

4. One baby had a cataract.

5. One baby had hypospadius. This case was removed from the series by the doctors who originated the study since they were not sure if the patient actually received cortisone. However, the case is included since it was given to us in the original thirty cases.

The mother of the baby with heart disease stated that one member of her family had congenital heart disease, and the mother whose baby had the cataract stated that one member of her family also had a cataract. We were unable to do follow-up studies on their families.

Although this series of cases was small, the end results on the fetus in the five cases cited were poor. Whether or not this small series represents extremely poor sampling, or whether cortisone was responsible for the end results is unknown. However, we feel justified on the above basis in suggesting that cortisone not be administered indiscriminately during the first trimester of pregnancy at this time. Future study may prove this wrong, but certainly caution is warranted for the present.

JOSEPH A. GUILBEAU, JR., CAPT., USAF (MC)

DEPARTMENT OF OBSTETRICS AND GYNECOLOGY
USAF HOSPITAL, MAXWELL AFB, ALA.
NOVEMBER 7, 1952

Items

American Board of Obstetrics and Gynecology

The American Board of Obstetrics and Gynecology will hold the next scheduled examinations (Part II), oral and pathological, for all candidates at the Edgewater Beach Hotel, Chicago, Ill., May 17 through May 24, 1953. Formal notice of the exact time of each candidate's examination will be sent him several weeks in advance of the examination dates. Requests for re-examination in Part II must be made prior to Feb. 1, 1953, submitting data regarding additional training or experience and medical school or hospital staff appointments acquired in the interim.

Inquiries relative to residency training should hereafter be directed to Lawrence M. Randall, M.D., Assistant Secretary, American Board of Obstetrics and Gynecology, Mayo Clinic, Rochester, Minn., who is in charge of residency training for the Board.

Application forms for Appraisal of Incomplete Training, for Certification, and requests for current Bulletins should be made to:

> ROBERT L. FAULKNER, M.D., SECRETARY,
> AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY
> 2105 ADELBERT ROAD
> CLEVELAND 6, OHIO

Second Annual Obstetrical Gynecological Forum

The Second Annual Obstetrical Gynecological Forum, sponsored by the Los Angeles Obstetrical and Gynecological Society, will be held at the Elks Club on February 14 and 15, for all interested licensed physicians. An outstanding program by prominent authorities, including N. S. Assali of Cincinnati, Bayard Carter of Durham, M. Edward Davis of Chicago, Ludwig Emge of San Francisco, and Robert H. Williams of Seattle, is planned. All general practitioners will receive credit from their academy for attending this excellent symposium. Reservations may be made with Dr. John Gaspar, 6253 Hollywood Blvd., Hollywood, Calif.

Roster of American Obstetrical and Gynecological Societies

Hereafter the Roster will be published in January and July only. Changes, omissions, and corrections should be sent to the publishers, The C. V. Mosby Company, 3207 Washington Blvd., St. Louis 3, Mo.

ROSTER OF AMERICAN OBSTETRICAL AND GYNECOLOGICAL
SOCIETIES*

(Appears in January, April, July, October)

American Academy of Obstetrics and Gynecology. (1945) *President,* Carl P. Huber, Indianapolis, Ind. *Secretary,* Ralph A. Reis, 116 S. Michigan Ave., Chicago 3, Ill.

American Gynecological Society. (1876) *President,* William P. Healy, New York, *Secretary,* John I. Brewer, 104 S. Michigan Ave., Chicago 3, Ill. Next meeting, Lake Placid Club, Essex County, New York, June 15, 16, and 17, 1953.

American Association of Obstetricians, Gynecologists and Abdominal Surgeons. (1888) *President,* Nicholson J. Eastman, Baltimore, Md. *Secretary,* William F. Mengert, 2211 Oak Lawn, Dallas 4, Texas. Annual meeting at Hot Springs, Va., Sept. 10, 11, and 12, 1953.

Central Association of Obstetricians and Gynecologists. (1929) *President,* John I. Brewer, Chicago, Ill. *Secretary,* Harold L. Gainey, 116 S. Michigan Ave., Chicago 3, Ill. Annual meeting, Memphis, Tenn., Oct. 30, 31, and Nov. 1, 1952.

South Atlantic Association of Obstetricians and Gynecologists. (1938) *President,* Francis Bayard Carter, Durham, N. C. *Secretary,* John C. Burwell, Jr., 101 N. Elm, Greensboro, N. C. Next meeting, Havana, Cuba, Jan. 29 through Feb. 1, 1953.

A. M. A. Section on Obstetrics and Gynecology. *Chairman,* Arthur B. Hunt, Rochester, Minn. *Secretary,* Bernard J. Hanley, 1930 Wilshire Blvd., Los Angeles, Calif. Next meeting, New York, N. Y., June, 1953.

Society of Obstetricians and Gynaecologists of Canada. (1944) *President,* W. P. Tew, London, Ont. *Secretary,* G. A. Simpson, Royal Victoria Hospital, Montreal, P. Q. Next meeting, Thousand Islands Club, Alexandria Bay, New York, U. S. A., June 5, 6, and 7, 1953.

Akron Obstetrical and Gynecological Society. (1946) *President,* Donald C. Snyder. *Secretary,* Robert M. DeWitt, 159 S. Main St., Akron 8, Ohio. Meetings, October, January, April, and July, third Friday of month.

Alabama Obstetrical and Gynecological Association. (1940) *President,* J. R. Garber. *Secretary,* Herbert H. Thomas, 920 S. 19 St., Birmingham. Meetings, October and April.

Alameda County Gynecological Society. (1951) *President,* Ernest W. Henderson. *Secretary,* Charles F. Lewis, 3023 Summit St., Oakland, Calif. Meetings, third Wednesday each month.

Birmingham Obstetrical and Gynecological Society. (1949) *President,* M. Y. Dabney. *Secretary,* Wade Cline, 2205 Highland Ave., Birmingham. Meetings, September, December, February, and May.

Boston, Obstetrical Society of. (1861) *President,* George W. Waterman. *Secretary,* A. Gordon Gauld, 1180 Beacon St., Brookline 46, Mass. Meetings, Oct. 21, Nov. 18, 1952, Jan. 20, Feb. 17, March 17, and April 21, 1953 (Tri-City Meeting).

Bronx Gynecological and Obstetrical Society. (1924) *President,* Benjamin Karen. *Secretary,* Alex Charlton, 1749 Grand Concourse, New York 53, N. Y. Meetings, fourth Monday, October through April.

Brooklyn Gynecological Society. (1890) *President,* Charles H. Loughran. *Secretary,* Leslie H. Tisdall, 615 Third St., Brooklyn 15, N. Y. Meetings, third Wednesday, October through May.

Buffalo Obstetrical and Gynecological Society. (1946) *President,* Clyde L. Randall. *Secretary,* Louis A. Trippe, 511 Lafayette Ave., Buffalo. Meetings, first Tuesday, October through May, Saturn Club.

Central New York Association of Gynecologists and Obstetricians. (1938) *President,* Michael J. Elwood. *Secretary,* Vincent J. Hemmer, 713 E. Genesee St., Syracuse. Meetings, third Tuesday, September, November, January, March, and May.

Chicago Gynecological Society. (1878) *President,* Edward M. Dorr. *Secretary,* Edwin J. DeCosta, 104 S. Michigan Ave., Chicago 3, Ill. Meetings, third Friday, October through June, Hotel Knickerbocker.

Cincinnati Obstetrical Society. (1876) *President,* Joseph Crotty. *Secretary,* Robert R. Pierce, 116 William Howard Taft Rd., Cincinnati 19. Meetings, third Thursday, September through June.

Cleveland Society of Obstetrics and Gynecology. (1947) *President,* G. B. Hurd. *Secretary,* G. Keith Folger, 10515 Carnegie Ave., Cleveland 6. Meetings, fourth Monday, September, November, January, March, and May.

Columbus Obstetrical and Gynecological Society. (1944) *President,* Richard L. Meiling. *Secretary,* Leonard B. Greentree, 350 E. Broad St., Columbus 15. Meetings, last Wednesday of month, September through May.

Dallas-Fort Worth Obstetric and Gynecological Society. (1948) *President,* W. P. Devereux. *Secretary,* Oran V. Prejean, 4317 Oak Lawn Ave., Dallas 19. Meetings, spring and fall.

Dayton Obstetrical and Gynecological Society. (1937) *President,* E. W. Smith. *Secretary,* H. E. McKnight, Fidelity Bldg., Dayton. Meetings, third Wednesday, September through May.

Denver Gynecological and Obstetrical Society. (1942) *President,* Cuthbert Powell. *Secretary,* Gerard W. del Junco, 2025 E. 18 Ave., Denver 6. Meetings, first Monday of month, September through June.

El Paso Gynecological Society. (1948) *President,* Erich Spier. *Secretary,* Alvin L. Perry, Medical Arts Bldg., El Paso, Texas. Annual meeting, Jan. 15, 1953. Others arranged.

Florida Obstetric and Gynecologic Society. (1948) *President,* Dorothy D. Brame. *Secretary,* J. C. Taylor, 1022 Park St., Jacksonville. Meetings, December and April.

Georgia State Obstetrical and Gynecological Society. (1951) *President,* George Williams, Atlanta. *Secretary,* Jule C. Neal, Jr., 101 Professional Bldg., Macon. Meetings semiannually.

Honolulu Obstetrical and Gynecological Society. (1947) *President,* Lyle G. Phillips. *Secretary,* James T. S. Wong, 1415 Kalakaua Ave. Meetings, third Monday of each month at the Mabel Smyth Memorial Bldg.

Houston Obstetrical and Gynecological Society. (1939) *President,* E. A. Chandler. *Secretary,* J. T. Armstrong, 6410 Fannin, Houston 25. Meetings, first Tuesday each month, October through June.

Indianapolis Obstetrical and Gynecological Society. (1947) *President,* J. William Hofmann. *Secretary,* C. O. McCormick, Jr., 621 Hume Mansur Bldg., Indianapolis 4. Meetings, January, April, and October.

Interurban Obstetrical and Gynecological Society. (1949) *President,* Thomas Noble. *Secretary,* E. R. Duggan, 16 N. Goodman St., Rochester 7, N. Y. Meeting, October 11, 1952, Albany, N. Y.

Iowa Obstetric and Gynecologic Society. *President,* E. V. Edwards. *Secretary,* William C. Keettel, 343 Hutchinson, Iowa City. Meetings, spring and fall.

Kansas City Gynecological Society. (1922) *President,* Alexander B. Sinclair, Jr. *Secretary,* James E. Keeler, 4301 Main St., Kansas City, Mo. Meetings, Sept. 25, Nov. 13, 1952, Jan. 29, March 26, and May 7, 1953.

Kentucky Obstetrical and Gynecological Society. (1947) *President,* Clyde Sparks, Ashland. *Secretary,* J. B. Marshall, Louisville.

Los Angeles Obstetrical and Gynecological Society. (1914) *President,* E. W. Cartwright. *Secretary,* A. N. Webb, 3130 W. 6 St., Los Angeles 5. Meetings, second Tuesday, September, November, January, March, and May.

Louisville Obstetrical and Gynecological Society. *President,* Bruce B. Mitchell. *Secretary,* William Procter Eubank, Heyburn Bldg., Louisville. Meetings monthly.

Madison Obstetrical and Gynecological Society. (1950) *President,* Fred A. Brawn, 110 E. Main St., Madison, Wis. Meetings, first Tuesday each month except July, August, and September.

Maryland, Obstetrical and Gynecological Society of. (1929) *President,* John Savage, Baltimore. *Secretary,* W. Drummond Eaton, 11 E. Chase St., Baltimore 2. Meetings, second Thursday, October, December, February, and April.

Memphis Obstetrical and Gynecological Society. (1950) *President,* M. J. Roach, Jr. *Secretary,* William F. Mackey, 1374 Madison Ave., Memphis, Tenn. Meetings, fourth Friday, October through May.

Miami Obstetrical and Gynecological Society. (1946) *President,* Ralph Jack. *Secretary,* Henry Caffee, Douglas Entrance, Coral Gables. Meetings, second Thursday, January, March, May, and November.

Michigan Society of Obstetricians and Gynecologists. (1924) *President,* Harold H. Lampman. *Secretary,* C. Paul Hodgkinson, 2799 W. Grand Blvd., Detroit 2. Meetings, first Tuesday, October through May.

Minnesota Obstetrical and Gynecological Society. *President,* John A. Haugen. *Secretary,* Rodney F. Sturley, 350 Saint Peter St., St. Paul. Meetings, spring and fall.

Mississippi Obstetrical and Gynecological Society. (1947) *President,* William B. Wiener, Jackson. *Secretary,* J. A. K. Birchett, Street Clinic, Vicksburg. Meetings semiannually.

Mobile Obstetrical and Gynecological Society. (1949) *President,* G. J. Mitchell. *Secretary,* A. J. Brown, 57 St. Francis St., Mobile, Ala. Meetings, second Thursday, January, April, July, and October.

Montana Obstetrical and Gynecological Society. (1946) *President,* Earl L. Hall. *Secretary,* H. W. Fuller, Great Falls Clinic, Great Falls. Meetings, spring and fall.

Nassau Obstetrical Society. (1944) *President,* Carl J. McKenna. *Secretary,* Gerald T. Lilly, 821 Franklin Ave., Garden City, N. Y. Meetings, second Monday of the month.

New England Obstetrical and Gynecological Society. (1929) *President,* Joel M. Melick, Worcester, Mass. *Secretary,* Carmi R. Alden, 270 Commonwealth Ave., Boston 16, Mass. Meetings held in May and October.

New Jersey Obstetrical and Gynecological Society. (1947) *President,* Robert A. MacKenzie. *Secretary,* Felix H. Vann, 242 Engle St., Englewood. Meetings semiannually.

New Mexico Obstetrical and Gynecological Society. (1947) *President,* C. S. Shortle. *Secretary,* W. E. Rapp, 4800 Gibson Ave., S.E., Albuquerque. Meetings, October, November, January, March, and May.

New Orleans Obstetrical and Gynecological Society. (1924) *President,* Curtis Tyrone. *Secretary,* Abe Golden, 1522 Aline St., New Orleans. Meetings held October, November, January, March, and May.

New York Obstetrical Society. (1863) *President,* Samuel A. Cosgrove. *Secretary,* Henry S. Acken, Jr., 34 Prospect Park West, Brooklyn 15. Meetings, second Tuesday from October through May.

North Carolina Obstetrical and Gynecological Society. (1932) *President,* C. H. Mauzy, Jr., Winston-Salem. *Secretary,* Adam Thorpe, Rocky Mount. Meetings, December and April.

North Dakota Society of Obstetrics and Gynecology. (1938) *President,* Carl Baumgartner. *Secretary,* John Gillam, 807 Broadway, Fargo, N. D. Meetings, spring and fall.

Northeastern New York Obstetrical and Gynecological Society. (1935) *President,* Thomas Gamble. *Secretary,* Rudolph F. Amyot, 71 Second St., Troy, N. Y. Meetings, third Thursday of January, May, and October.

Oklahoma City Obstetrical and Gynecological Society. (1940) *President,* John M. Parrish, Jr. *Secretary,* John F. Daniel, Medical Arts Bldg. Meetings bimonthly, September through May.

Omaha Obstetrical and Gynecological Society. (1947) *President,* John Grier. *Secretary,* Leland Olson, 1107 Medical Arts Bldg., Omaha 2, Neb. Meetings, third Wednesday, January, March, May, September, and November.

Oregon Society of Obstetricians and Gynecologists. *President,* James M. Whitely. *Secretary,* William O. Thomas, Jr., 1735 N. Wheeler Ave., Portland 12. Meetings, third Friday, October through May.

Pacific Coast Obstetrical and Gynecological Society. (1931) *President,* Karl L. Schaupp, San Francisco 2. *Secretary,* Donald G. Tollefson, 511 S. Bonnie Brae St., Los Angeles 5, Calif. Meeting, Oct. 15-18, 1952, Del Monte, Calif.

Pacific Northwest Obstetrical and Gynecological Association. (1947) *President,* J. Ross Vant, Edmonton, Alberta, Canada. *Secretary,* R. D. Reekie, W. 407 Riverside Ave., Spokane 8, Wash. Meeting, June 28-July 1, 1953, Jasper Park Lodge, Alberta, Canada.

Philadelphia, Obstetrical Society of. (1868) *President,* J. Marsh Alesbury. *Secretary,* Paul O. Klingensmith, 133 S. 36 St., Philadelphia 4. Meetings, first Thursday, October through May.

Pittsburgh Obstetrical and Gynecological Society. (1934) *President,* A. C. Williamson. *Secretary,* William E. Gibson, 1010 Center St., Pittsburgh 21. Meetings, first Monday, October, November, December, February, March, April, and May.

Portland Society of Obstetricians and Gynecologists. *President,* R. D. Blatchford. *Secretary,* George H. Lage, 453 Medical Arts Bldg., Portland 5. Meetings, fourth Wednesday, September through May.

Queens Gynecological Society. (1948) *President,* Sanford Kaminester. *Secretary,* George Schaefer, 112-25 Queens Blvd., Forest Hills, N. Y. Meetings, second Wednesday, October, December, February, and April.

Rochester Obstetrical and Gynecological Society. (1939) *President,* W. T. Pommerenke. *Secretary,* John Schultz, Rochester, N. Y. Meetings, September, December, March, and June.

St. Louis Gynecological Society. (1924) *President,* Carl Wegner. *Secretary,* J. Russell Vaughan, 634 N. Grand Blvd., St. Louis 3, Mo. Meetings, second Thursday, October, December, February, and April.

San Antonio Obstetrical and Gynecological Society. *President,* G. G. Passmore. *Secretary,* Frank M. Posey, Jr., 640 Moore Bldg. Meetings, first Monday of the month.

San Diego Gynecological Society. (1937) *President,* John W. Wanless. *Secretary,* James Ravenscroft, Juniper and First Avenues, San Diego. Meetings, fourth Friday of each month.

San Francisco Gynecological Society. (1929) *President*, Chester L. Cooley. *Secretary*, Edmund F. Anderson, 2445 Ocean Ave., San Francisco 27. Meetings, second Friday, October through April, Sir Francis Drake Hotel, San Francisco, or Claremont Country Club, Oakland.

Seattle Gynecological Society. (1941) *President*, Hugh Nuckols. *Secretary*, Robert H. Stewart, Seattle. Meetings, third Wednesday of each month, September through June, except February, Washington Athletic Club.

South Carolina Obstetrical and Gynecological Society. (1946) *President*, Wesley J. Snyder, Jr. *Secretary*, Frank B. C. Geibel, 1517 Hampton St., Columbia 1.

Southwest Obstetrical and Gynecological Society. (1951) *President*, Preston T. Brown, Phoenix, Ariz. *Secretary*, Jesse A. Rust, Jr., 3115 University Ave., San Diego, Calif. Annual fall meeting, Nov. 14 and 15, 1952, Tucson, Ariz.

Texas Association of Obstetricians and Gynecologists. (1930) *President*, George Adam. *Secretary*, Carey Hiett, 815 Fifth Ave., Ft. Worth. Meeting, Feb. 13 and 14, 1953, Hilton Hotel, Ft. Worth.

Utah Obstetrical and Gynecological Society. (1948) *President*, M. S. Sanders. *Secretary*, Linwood Smith, Boston Bldg., Salt Lake City. Meetings, second Thursday, October, December, March, and May.

Virginia Obstetrical and Gynecological Society. (1936) *President*, Henry C. Spalding. *Secretary*, Chester D. Bradley, 2914 West Ave., Newport News, Va. Meetings, April and October.

Washington Gynecological Society. (1933) *President*, Andrew A. Marchetti. *Secretary*, J. Keith Cromer, 1801 Eye St., N.W., Washington, D. C. Meetings, fourth Saturday, October, November, January, March, and May.

Washington State Obstetrical Association. (1936) *President*, C. W. Knudson. *Secretary*, L. Bruce Donaldson, 532 Stimson Bldg., Seattle 1. Meetings, spring and fall.

Wisconsin Society of Obstetrics and Gynecology. (1940) *President*, Fred J. Hofmeister. *Secretary*, Alice D. Watts, 324 E. Wisconsin Ave., Milwaukee. Meetings, May and October.